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(54) Catalytic domain of the human effector cell cycle checkpoint protein kinase, Chk1, materials and methods for identification of inhibitors thereof

(57) The present invention relates to the identification, isolation and purification of the catalytic domain of the human effector checkpoint protein kinase (hChk1). A 1.7Å crystal structure of the hChk1 kinase domain in the active conformation is reported herein. The kinase domain of hChk1 and its associated crystal structure is described for use in the discovery, identification and characterization of inhibitors of hChk1. This structure provides a three-dimensional description of the binding site of the hChk1 for structure-based design of small molecule inhibitors thereof as therapeutic agents. Inhibitors of hChk1 find utility in the treatment of hyperproliferative disorders such as HIV and cancer.

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Description

[0001] This application claims priority from co-pending United States Provisional Application Serial Number 60/162,887, filed November 1, 1999, the contents of which are incorporated by reference herein in their entirety.

FIELD OF THE INVENTION

[0002] The present invention generally relates to cell cycle checkpoint kinases which are essential to cellular DNA damage responses and coordinating cell cycle arrest. The checkpoint kinases play a role in the surveillance and response to DNA damage. The damage may result from external or internal forces. Such forces include but are not limited to errors in replication, DNA base damage, DNA strand breaks, or exposure to radiation or cytotoxic chemicals. These checkpoint kinases are integral in the regulatory pathways leading to cell cycle arrest and apoptosis following DNA damage, giving the cell notice and time to correct lesions prior to the initiation of replication and chromosome separation. The present invention more specifically relates to the isolation and purification of the catalytic domain of the human effector checkpoint protein kinase (hChk1) and its use in the discovery, identification and characterization of inhibitors of same.

BACKGROUND

[0003] Cell growth, division and death is essential to the life cycle of multi-celled organisms. These processes and their regulation are strikingly similar across all eukaryotic species. Somatic cell division consists of two sequential processes: DNA replication followed by chromosomal separation. The cell spends most of its time preparing for these events in a growth cycle (interphase) which in turn consists of three subphases: initial gap (G_1), synthesis (S), and secondary gap (G_2). In G_1, the cell, whose biosynthetic pathways were slowed during mitosis, resumes a high rate of biosynthesis. The S phase begins when DNA synthesis starts and ends when the DNA content of the nucleus has doubled. The cell then enters G_2, which lasts until the cell enters the final phase of division, mitotic (M). The M phase begins with nuclear envelope breakdown, chromosome condensation and formation of two identical sets of chromosomes which are separated into two new nuclei. This is followed by cell division (cytokinesis) in which each nuclei is separated into two daughter cells, which terminates the M phase and marks the beginning of interphase for the new cells.

[0004] The sequence in which the cell cycle events proceed is tightly regulated such that the initiation of one cell cycle event is dependent upon the successful completion of the prior cell cycle event. The process of monitoring genome integrity and preventing cell cycle progress in the event of DNA damage has been described as a 'cell cycle checkpoint' (Hartwell, LH et at., *Science*, **246**:629-634 (1989); Weinert et al., *Genes and Dev.*, **8**:652 (1994)]. Cell cycle checkpoints consist of signal transduction cascades which couple DNA damage detection to cell cycle progression. Checkpoints are control systems that coordinate cell cycle progression by influencing the formation, activation and subsequent inactivation of the cyclin-dependent kinases. Checkpoint enzymes are responsible for maintaining the order and fidelity of events of the cell cycle by blocking mitosis in response to unreplicated or damaged DNA. These enzymes prevent cell cycle progression at inappropriate times, maintain the metabolic balance of cells while the cell is arrested and in some instances can induce apoptosis (programmed cell death) when the requirements of the checkpoint have not been met (O'Connor, PM, *Cancer Surveys*, **29**, 151-182 (1997); Nurse, P, *Cell*, **91**, 865-867 (1997); Hartwell, LH et al, *Science*, **266**, 1821-1828 (1994); Hartwell, LH et al., *Science*, **246**, (1989), supra).

[0005] One series of checkpoints monitors the integrity of the genome. Upon sensing DNA damage, these "DNA damage checkpoints" block cell cycle progression in G_1 & G_2 phases, and slow progression through S phase (O'Connor, PM, *Cancer Surveys*, **29** (1997), supra; Hartwell, LH et at, *Science*, **266**, (1994), supra). This action enables DNA repair to be completed before replication of the genome and subsequent separation of this genetic material into new daughter cell takes place.

[0006] Various mutations associated with malignancy affect the cancer cells ability to regulate checkpoints, allowing cells with DNA damage the increased likelihood to continue replicating and to escape damage-mediated apoptosis These factors contribute to the genomic instability which drives the genetic evolution of human cancers and contributes to the resistance of cancer cells to most current chemotherapy and radiotherapy intervention.

[0007] Due to abnormalities in the p53 tumor suppressor pathway, most cancer cells lack a functional G_1 checkpoint control system. This makes them particularly vulnerable to abrogation of the last remaining barrier protecting them from the cancer killing effects of DNA damaging agents: the G_2 checkpoint. The G_2 DNA damage checkpoint ensures maintenance of cell viability by delaying progression into mitosis in cells that have suffered genomic damage. The G_2 checkpoint is controlled by cell cycle checkpoint pathways which inhibit mitosis if previous events are incomplete or if the DNA is damaged. This regulation control system has been conserved from yeast to humans. Important in this conserved system is a kinase, Chk1 (or p56Chk1), which transduces signals from the DNA damage sensory complex to inhibit activation of the cyclin B/Cdc2 kinase which promotes mitotic entry (Peng, CY et al, *Science*, **277**, 1501-1505

(1997); Sanchez Y, et al., *Science*, **277**, 1497-1501 (1997); Walworth, N et al., *Nature*, **363**(6427), 368-71 (May 27, 1993); al-Khodairy et al., *Mol Biol Cell*, **5**(2):147-60 (Feb, 1994); Carr et al., *Curr Biol.*, **5**(10): 1179-90 (Oct. 1, 1995)). The repair checkpoint kinase, Chk1, regulates Cdc25, a phosphatase that activates Cdc2. Thus, Chk1 serves as the direct link between the G_2 checkpoint and the negative regulation of Cdc2.

[0008] Inactivation of Chk1 has been shown to both abrogate G_2 arrest induced by DNA damage inflicted by either anticancer agents or endogenous DNA damage, as well as, result in preferential killing of the resulting checkpoint defective cells (Nurse, P, *Cell*, **91**, (1997), supra; Weinert, T, *Science*, **277**, 1450-1451 (1997); Walworth, N et al., *Nature*, **363**, (1993) supra; al-Khodairy et al., *Molec. Biol. Cell*, **5**, (1994), supra; Wan, S et al., *Yeast*, **15**(10A), 821-8 (Jul. 1999)).

[0009] The fact that cancer cells have also been shown to be more vulnerable to G_2 checkpoint abrogation has encouraged the pursuit of G_2 checkpoint abrogating drugs (Wang, Q et al., *PNAS* **96**: 3706-3711 (1999); Fan, S et al., *Cancer Res.*, **55**, 1649-1654 (1995); Powell, SN et al., *Cancer Res.*, **55**, 1643-1648 (1995); Russell, KJ et al., *Cancer Res.*, **55**, 1639-1642 (1995); Wang, Q et al., *J Natl Cancer Inst.*, **88**, 956-967 (1996)). Such checkpoint abrogating drugs could improve the killing of tumors exposed to DNA damaging events including that inflicted by therapeutic agents, hypoxic-stress induced because of a limited blood supply (anti-angiogenic agents), or endogenous DNA damage arising as a consequence of a cancer cell's inherent genomic instability. Selective manipulation of checkpoint control in cancer cells can afford broad utilization in cancer chemotherapeutic and radiotherapy regimens and may in addition, offer a common hallmark of human cancer "genomic instability" to be exploited as the selective basis for the destruction cancer cells.

[0010] A number of lines of evidence place Chk1 as a pivotal target in DNA damage checkpoint control. However, Chk1 is a difficult enzyme to study because the full length protein is not the most active form of Chk1. While others have examined the nucleotide and amino acid sequence of the full-length checkpoint kinase and estimated the location of the kinase domain, there is a need for the isolation and purification of the kinase domain of Chk1 and the maintenance of its catalytically active conformation.

SUMMARY OF THE INVENTION

[0011] The generation, kinetic characterization, and structure determination of the kinase domain of the human Chk1 protein is disclosed herein. The domain begins between residues 1 and 16 and terminates between residues 265 and 291 of the full length protein [**SEQ ID NO. 2**] which comprises 476 amino acids. The domain preferably extends from residues 1-265, more preferably from residues 1-289.

[0012] The invention relates to an isolated, purified polynucleotide which encodes the active conformation of the human Chk1 kinase or an active kinase analog thereof. The polynucleotide may be natural or recombinant.

[0013] The invention also relates to an isolated, soluble catalytically active polypeptide comprising the active conformation of the human Chk1 kinase or an active kinase analog thereof.

[0014] The invention encompasses both the polypeptide *per se* as well as salts thereof. As discussed in detail below, a high salt concentration (about 500 mM) in the buffer is used herein to prevent aggregation of peptide during purification and storage.

[0015] The invention also relates to a crystal structure of the human Chk1 kinase in the active conformation resolved to at least 2.5Å, preferably 2.0Å, more preferably 1.7Å. This structure provides a three-dimensional description of the target (human Chk1) for structure-based design of small molecule inhibitors thereof as therapeutic agents.

[0016] The invention further relates to an expression vector for producing catalytically active human Chk1 kinase in a host cell.

[0017] The invention further relates to a host cell stably transformed and transfected with a polynucleotide encoding of the human Chk1 kinase, or fragment thereof; or an active kinase analog thereof, in a manner allowing the expression of the human Chk1 kinase in the active configuration.

[0018] The present invention further discloses methods for screening candidate compounds using the molecular structure of the x-ray crystallography data to model the binding of candidate compounds.

[0019] The invention further provides a method for designing and screening potentially therapeutic compounds for the treatment of hyper-proliferative or diseases related to proliferation, including but not limited to cancer and HIV infection. The putative therapeutics can be screened for activities such as (1) potentiation of the cytotoxicity of DNA damaging agents such as synthetic or natural chemotherapeutic agents and ionizing or neutron radiation; (2) enhancement of the cytotoxicity of DNA synthesis inhibitors including antimetabolites, DNA chain terminators, or other mechanisms that would lead to the inhibition of DNA synthesis; (3) enhancement of the cytotoxicity of hypoxia as would occur within tumors due to a limited blood supply; and (4) inhibition of the ability of HIV to arrest cell cycle progression such as that induced by the VPR protein. Compounds that inhibit human Chk1 kinase activity or abrogate the G2 checkpoint can be used to treat or prevent the hyperproliferation associated with cancer and HIV.

[0020] The present invention provides methods for identifying potential inhibitors of the human Chk1 protein kinase by *de novo* design of novel drug candidate molecules that bind to and inhibit human Chk1 protein kinase activity, or that improve their potency. The x-ray crystallographic coordinates disclosed herein, allow generation of 3-dimensional models of the catalytic site and the drug binding site of the human Chk1 protein. *De novo* design comprises of the generation of molecules via the use of computer programs which build and link fragments or atoms into a site based upon steric and electrostatic complementarily, without reference to substrate analog structures. The drug design process begins after the structure of the target (human Chk1 kinase) is solved to at least a resolution of 2.5__. Refinement of the structure to a resolution of 2.0 Å or better with fixed water molecules in place provides more optimal conditions to undertake drug design.

[0021] The invention further provides a method for computational modeling of the kinase domain of human Chk1, such a model being useful in the design of compounds that interact with this domain. The method involves crystallizing the Chk1 kinase in the catalytically active configuration; resolving the x-ray structure of said active kinase, particularly the kinase domain and binding site of active Chk1; and applying the data generated from resolving the x-ray structure to a computer algorithm capable of generating a three dimensional model of the kinase domain and binding site suitable for use in designing molecules that will act as agonists or antagonists to the polypeptide. An iterative process can then be applied to various molecular structures using the computer-generated model to identify potential agonists or antagonists of the Chk1 kinase. Inhibitors of the kinase can serve as lead compounds for the design of potentially therapeutic compounds for the treatment of diseases or disorders associated with hyperproliferation or related to proliferation, such as cancer and HIV.

[0022] The invention further provides a process where the human Chk1 protein kinase is modified by deletion of the C-terminal portion of the protein so as to impart favorable physical characteristics of the resulting polypeptide. The kinase domain is suitable for analysis by nuclear magnetic resonance, high throughput screening, biochemical characterizations, x-ray crystallography, colorimetry and other diagnostic means. The most preferred deletion fragment extends from residue 1 to residue 289.

[0023] The invention further provides screening methods for use in the drug design process of potential agents to the human Chk1 protein kinase by *de novo* design of novel drug candidate molecules with potentially nanomolar potencies. The x-ray crystallographic coordinates disclosed based on the kinase domain of the human Chk1 protein will allow the generation of 3-dimensional models of the active binding sites of the human Chk1 protein.

[0024] The invention further provides a method for rapidly screening compounds to identify those compounds that inhibit Chk1 kinase or core structure for further Chk1 inhibitor design. The high throughput-screening assay is capable of being fully automated on robotic workstations. The assay may be radioactive. However, in a preferred embodiment the assay is a non-radioactive ELISA. In a more preferred embodiment, the assay is an ELISA that utilizes a novel antibody, rabbit anti-phosphosyntide, to specifically detect the product of the Chk1 kinase reaction in which biotin-syntide is the substrate. However, the basis of the assay includes the ability to use other substrates detectable by anti-phosphopeptide/ protein antibodies. The assay may be used to screen large collections of compound libraries to discover Chk1 kinase inhibitors and potential lead compounds for the development of Chk1 kinase selective anticancer compounds. The assay finds utility in the screening of other syntide substrate kinase reactions involving kinases of analogous activity to Chk1.

BRIEF DESCRIPTION OF THE DRAWINGS

[0025]

Figure 1. The G_2 DNA damage checkpoint mechanism in fission yeast (Furnari et al., *Science*, **277**: 1495-1497 (Sep. 5, 1997).

Figure 2. Sequence alignment of Chk1 kinase domains of human (hs) (SEQ ID NO: 2), mouse (mm) (SEQ ID NO: 18), Xenopus (xl) (SEQ ID NO: 19), fruit fly (dm) (SEQ ID NO: 20), C. elegans (ce) (SEQ ID NO: 21), S. cerevisiae (sc) (SEQ ID NO: 22), and S. pombe (sp) (SEQ ID NO: 23). Secondary structural elements of human Chk1 are shown above the alignment. The numbers of amino acids are shown on the right. Invariant residues among these species are in red and human Chk1 residues that also conserved in other species are in cyan.

Figure 3. The homology model of Chk1 kinase depicting the activation loop and its relationship to the catalytic loop and C helix. The Chk1 N and C-terminal lobes are shown. The fragments corresponding to the Chk1 C-helix are residues 50-58; the Chk1 catalytic loop are residues 129-132; and the Chk1 activation loop are residues 148-170.

Figure 4. The purification scheme for Chk1 kinase domain 1-289.

Figure 5. The structure of human Chk1 kinase domain identified using the crystal resolved to 1.7 Å. A ribbon diagram of the binary complex structure of Chk1 with AMP-PNP showing the secondary structural elements and the loops discussed in the text. The α-helices are shown in blue, the β-strands in cyan, the catalytic loop in orange, the activation loop in red. AMP-PNP and sulfate ion are shown as ball and stick models. The termini are denoted by N and C.

Figure 6. Catalytic site of Chk1. Cross section of the catalytic site of human Chk1 with AMP-PNP. Protein C α-ribbon representations are shown in purple for Chk1. The side chains of the catalytic site residues are shown as ball and stick models and are color-coded by atom type: carbon, green; nitrogen, blue; oxygen, red. The distances (__) along the dotted lines between the catalytic site residues are shown.

Figure 7. Molecular surface of the Chk1 with modeled CDC25C peptide. The molecular surface of Chk1 is colored as follows: basic side chains are shown in blue, acidic side chains in red, and non-polar side chains in violate. CDC25C peptide (residues 211-219) is shown as tick model and color-coded by atom type: carbon, green; nitrogen, blue; oxygen, red; sulfur, yellow.

Figure 8. Stereoview of representative electron density map. Figure 8A shows a stereoview of a representative portion of the experimental density at 1.5__ calculated to 3.0__ with the use of phases after solvent flattening. Superimposed on the density is the final refined model. Figure 8B shows a difference Fourier map calculated with native model-derived phases and coefficients IFO(AMP-PNP)I-IFO(native/apoenzyme)I to the diffraction of 1.7__ and contoured at 2.5__. The triphosphate moiety of AMP-PNP is disordered and is omitted from the model. No Mg^{2+} ions are observed.

Figure 9. Representation of the Chk1 binding sites, showing specifically the specificity pocket, the ATP binding site, and the Donor-Acceptor-Donor binding motif.

Figure 10. The high throughput ELISA protocol.

Figure 11. The Chk1 crystal coordinates for the apoenzyme (isolated active Chk1 — Figure 11A) and the binary complex (Chk1 complexed with AMP-PNP, an ATP analog — Figure 11B) including the coordinates of the fixed water molecules.

DETAILED DESCRIPTION OF THE INVENTION

[0026] DNA damage induces the arrest of the cell cycle at the G_2 checkpoint. The G_2 DNA damage checkpoint ensures maintenance of cell viability by delaying progression into mitosis in cells which have suffered genomic damage. The G_2 checkpoint is controlled by cell cycle checkpoint pathways which have been extensively studied (Hartwell, LH et al., *Science*, **246** (1989), supra; Nurse, P et al., *Nat Med*, 4 (10): 1103-6 (Oct 1998); Peng et al., *Science*, **277**, (1997), supra; Furnari et al., *Science*, **277**: 1495-1497 (Sep. 5, 1997); Zeng et al., *Nature* **395** (6701):507-510 (Oct. 1, 1998); Martinho et al., *EMBO J*, **17**(24):7239-49 (Dec. 15, 1998); Nakajo et al., *Dev. Biol*. **207**(2):432-44 (Mar. 15, 1999); Carr et al., *Curr Biol*., **5** (1995), supra). The model of the checkpoint mechanism in fission yeast is shown in **Figure 1**, Furnari, et al., *Science*, (1997), supra. As mentioned above, the regulation control system is highly conserved from yeast to humans.

[0027] DNA damage activates the checkpoint pathway by inhibiting the dephosphorylation of the mitotic kinase Cdc2 at the tyrosine-15 residue [Cdc2 (Y^{15}-PO_4)], thereby inhibiting its mitotic initiating activity and arresting the cell cycle. This process is referred to as inhibitory phosphorylation. In order for mitosis to proceed, Cdc2 must be dephosphorylated, returning it to its active form. Phosphorylated Cdc2 is the substrate of Cdc25. Cdc25 is a dual specificity protein phosphatase that controls entry into mitosis by dephosphorylating the protein kinase Cdc2. In fission yeast, DNA damage also results in the activation of Rad3, a kinase related to the ATM/ATR proteins. Rad3 initiates the Chk1 response; the phosphorylation of Chk1 is a Rad3 dependent process (Martinho et al., *EMBO J*, **17** (1998), supra; Furnari et al., *Science*, **277** (1997), supra). Phosphorylated (active) Chk1 phosphorylates the mitotic inducer Cdc25 at the serine-216 residue of human Cdc25 [Cdc25 (S^{216}-PO_4)]. Phosphorylation of Cdc25 inhibits the function of the phosphatase in the dephosphorylation of Cdc2, an event required for mitosis to proceed. Throughout interphase but not in mitosis, Cdc25 is phosphorylated at the serine-216 residue and bound to members of the highly conserved and ubiquitously expressed family of 14-3-3 proteins. Prevention of serine-216 phosphorylation prevents 14-3-3 binding, perturbing mitotic timing and allowing cells to escape the G_2 checkpoint arrest induced by either unreplicated DNA or radiation induced damage.

[0028] A majority of currently accepted cancer treatments involve the induction of DNA damage including the

administration of anticancer agents, chemotherapeutic agents, and radiation therapy. Cancer cells frequently become resistant to such therapies. It is suspected that such resistance is related to the innate ability of the cancer cells to arrest and repair the damage induced. If the cancer cell was unable to arrest and repair, mitosis would proceed with the DNA damage intact. The downstream result would presumably be cell death as a result of the DNA damage.

[0029] Treatments that include a mechanism for abrogating the endogenous checkpoint pathway and repair process would presumably be more effective in killing cancer cells. As many cancer cells already lack a G_1 checkpoint control system, a therapy that involved the inhibition of the G_2 checkpoint would presumably force the cancer cells to proceed through mitosis without any feedback arrest and repair process. Hence, there is a clear utility for the inhibition of the activity of Chk1, a pivotal kinase in the G_2 checkpoint pathway. As many of the same events that regulate the G_2 arrest subsequent to DNA damage also regulate the S phase delay following DNA damage, the inhibition of Chk1 finds utility in the regulation of S phase as well.

[0030] The human Chk1 sequence of amino acids 1 to 476 is available through GenBank. Full length or segments of human Chk1 cDNA corresponding to codon 1-427, 1-265, and 1-289 were separately amplified by PCR. Each was tagged at its 3'-end with six histidine codons and cloned into an expression plasmid for protein production using a Baculovirus/insect cell expression system. The protein was expressed in insect Hi-5 cells and purified by a combination of ion-exchange and affinity column chromatography. It was found that a high concentration of salt (~500 mM levels) was required for keeping the purified Chk1 kinase domain from forming a precipitate.

[0031] The kinase activity of the hChk1 was determined by monitoring the ADP production through enzymatic actions of pyruvate kinase and lactate dehydrogenase. The Chk1 kinase domain containing amino acids 1-289 showed higher enzymatic activity than the full length protein. Unlike the other forms of Chk1 which have proven difficult to work with (isolate, purify, crystallize, etc), the 1-289 kinase domain form of the human Chk1 enzyme facilitated crystallography, enzyme characterization, and high throughput screening of inhibitors. In particular, the Chk1 kinase domain was used to determine its 3-dimensional structure, which provides unique structural information for inhibitor design for therapeutic development.

[0032] As used herein, the abbreviation 'hChk1' refers to the polynucleotide encoding the human effector checkpoint kinase serving as a DNA damage/replication checkpoint kinase. The nucleic acid sequence of the polynucleotide encoding the full length protein of human Chk1 was published in Science by Sanchez et al. (*Science*, **277** (5331): 1497-1501 (1997)) and published in GenBank on September 9, 1997 (AF016582). The nucleic acid sequence described therein is provided herein, shown in **SEQ ID NO. 1**. The corresponding peptide sequence of the full length protein is provided herein, shown in **SEQ ID NO. 2**. This peptide sequence was submitted to GenBank by Flaggs et al. on November 3, 1997 and released on December 13, 1997 (AF032874). The protein kinase was further described by Flaggs et al. in Current Biology (*Curr. Biol.*, **7**(12):977-986, (1997)).

[0033] Using homology tools to examine the nucleotide and peptide sequence of Chk1, scientists have attempted to estimate the location of the kinase domain. However, the exact location of the catalytically active kinase domain has been difficult to experimentally determine, primarily as no one has ever reported isolating the kinase domain in its active configuration. Previous publications have indicated that the kinase domain extends from AA 16 to AA 264 (WO99/111795, published March 11, 1999, at page 7, line 3) of **SEQ ID NO. 2**.

[0034] We have found that the catalytic kinase domain begins between AA1 and 16 and terminates between AA265 and AA291 of **SEQ ID NO. 2**. We further discovered that vector-driven protein yield is dramatically increased when a fragment extending from AA1 to AA289 (dubbed KH289) is used.

[0035] There are 22 known amino acids but 64 possible permutations of nucleic acid triplets, called "codons". Many amino acids are specified by more than one codon, a phenomenon called degeneracy. Due to the degeneracy of the genetic code, there are many functionally equivalent nucleic acid sequences that can encode the same protein. The active human Chk1 kinase set forth in **SEQ ID NO.2** can clearly be encoded by multiple nucleotide sequences and is not limited to the cDNA sequence set forth in **SEQ ID NO. 1**. For example, both UUU and UUC code for a phenylalanine while serine is encoded by UCU, UCC, UCA, UCG, AGU, and AGC [Molecular Biology of the Gene, 4th edition, Watson, J.D. et al., editors (1987) at pages 437-438]. Functionally equivalent sequences can readily be prepared using known methods such as modified primer PCR, site-directed mutagenesis, and chemical synthesis. Such functional equivalents are within the scope of this invention.

[0036] In the examples of the present invention, the full length form of human Chk1 protein kinase (AA 1-476) is referred to as KH476. Fragments thereof are identified by the amino acid sequence. For example, the human Chk1 kinase domain (AA 1-289) is referred to as KH289 Other kinase domain sequences are referred to by amino acid numbering in a similar manner.

A. Peptides, Proteins and Antibodies

[0037] As used herein, the terms "kinase" and "protein kinase" refer to enzymes that catalyze the transfer of a phosphate residue from a nucleoside triphosphate to an amino acid side chain in selected targets. The covalent phosphor-

ylation in turn regulates the activity of the target protein. In addition, phosphorylation frequently acts as the signal that triggers a particular process or reaction, playing an integral part in cellular regulation and control mechanisms. Clearly, inappropriate or unregulated phosphorylation can result in errors in cell signaling and the associated cell cycle and regulation processes. Most protein kinases are highly substrate specific.

[0038] As used herein, a peptide is said to be "isolated" or "purified" when it is substantially free of homologous cellular material or chemical precursors or other chemicals. The peptides of the present invention can be purified to homogeneity or other degrees of purity. The level of purification will be based on the intended use.

[0039] In some uses, "substantially free of cellular material" includes preparations of the peptide having less than about 30% (by dry weight) other proteins (i.e., contaminating protein), less than about 20% other proteins, less than about 10% other proteins, or less than about 5% other proteins. When the peptide is recombinantly produced, it can also be substantially free of culture medium, i.e., culture medium represents less than about 20% of the volume of the protein preparation.

[0040] The language "substantially free of chemical precursors or other chemicals" includes preparations of the peptide in which it is separated from chemical precursors or other chemicals that are involved in its synthesis. In one embodiment; the language "substantially free of chemical precursors or other chemicals" includes preparations of the kinase peptide having less than about 30% (by thy weight) chemical precursors or other chemicals, preferably less than about 20% chemical precursors or other chemicals, more preferably less than about 10% chemical precursors or other chemicals, or most preferably less than about 5% chemical precursors or other chemicals.

[0041] The isolated kinase described herein can be purified from cells that naturally express it, purified from cells that have been altered to express it (recombination), or synthesized using known protein synthesis methods. For example, a nucleic acid molecule encoding the protein kinase is cloned into an expression vector, the expression vector introduced into a host cell and the protein expressed in the host cell. The protein can then be isolated from the cells by an appropriate purification scheme using standard protein purification techniques. Many of these techniques are described in detail below.

[0042] The present invention also provides catalytically active variants of the peptides of the present invention, such as allelic/sequence variants of the peptides, non-naturally occurring recombinantly derived variants of the peptides, and orthologs and paralogs of the peptides. Such variants can be generated using techniques that are known by those skilled in the fields of recombinant nucleic acid technology and protein biochemistry.

[0043] Such variants can readily be identified/made using molecular techniques and the sequence information disclosed herein. Further, such variants can readily be distinguished from other peptides based on sequence and/or structural homology to the peptides of the present invention. The degree of homology/identity present will be based primarily on whether the peptide is a functional (active) variant or non-functional (inactive) variant, the amount of divergence present in the paralog family and the evolutionary distance between the orthologs.

[0044] To determine the percent identity of two amino acid sequences or two nucleic acid sequences, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in one or both of a first and a second amino acid or nucleic acid sequence for optimal alignment and non-homologous sequences can be disregarded for comparison purposes). In a preferred embodiment, the length of a reference sequence aligned for comparison purposes is at least 30%, 40%, 50%, 60%, 70%, 80%, or 90% or more of the length of the reference sequence. The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position (as used herein amino acid or nucleic acid 'identity' is equivalent to amino acid or nucleic acid 'homology'). The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, taking into account the number of gaps, and the length of each gap, which need to be introduced for optimal alignment of the two sequences.

[0045] The comparison of sequences and determination of percent identity and similarity between two sequences can be accomplished using a mathematical algorithm. (*Computational Molecular Biology*, Lesk, A.M., ed., Oxford University Press, New York, 1988; *Biocomputing: Informatics and Genome Projects*, Smith, D.W., ed., Academic Press, New York, 1993; *Computer Analysis of Sequence Data, Part 1*, Griffin, A.M., and Griffin, H.G., eds., Humana Press, New Jersey, 1994; *Sequence Analysis in Molecular Biology*, von Heinje, G., Academic Press, 1987; and *Sequence Analysis Primer*, Gribskov, M. and Devereux, J., eds., M Stockton Press, New York, 1991). In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch (*J. Mol. Biol.* (48):444-453 (1970)) algorithm which has been incorporated into commercially available computer programs, such as GAP in the GCG software package, using either a Blossom 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences can be determined using the commercially available computer programs including the GAP program in the GCG software package (Devereux, J., *et al.*, *Nucleic Acids Res. 12(1)*:387 (1984)), the NWS gap DNA CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. In another embodiment, the percent identity between two amino acid or nucleotide sequences is determined using the algorithm

of E. Meyers and W. Miller (CABIOS, 4:11-17 (1989)) which has been incorporated into commercially available computer programs, such as ALIGN (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

[0046] The nucleic acid and protein sequences of the present invention can further be used as a "query sequence" to perform a search against sequence databases to, for example, identify other family members or related sequences. Such searches can be performed using commercially available search engines, such as the NBLAST and XBLAST programs (version 2.0) of Altschul, et at. (*J. Mol. Biol.* 215:403-10 (1990)). Nucleotide searches can be performed with such programs to obtain nucleotide sequences homologous to the nucleic acid molecules of the invention. Protein searches can be performed with such programs to obtain amino acid sequences homologous to the proteins of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al. (*Nucleic Acids Res.* 25(17):3389-3402 (1997)).

[0047] Full-length clones comprising one of the peptides of the present invention can readily be identified as having complete sequence identity to one of the kinases of the present invention as well as being encoded by the same genetic locus as the kinase provided herein.

[0048] Allelic variants of a peptide can readily be identified as having a high degree (significant) of sequence homology/identity to at least a portion of the peptide as well as being encoded by the same genetic locus as the kinase peptide provided herein. As used herein, two proteins (or a region of the proteins) have significant homology when the amino acid sequences are typically at least about 70-75%, 80-85%, and more typically at least about 90-95% or more homologous. A significantly homologous amino acid sequence, according to the present invention, will be encoded by a nucleic acid sequence that will hybridize to a peptide encoding nucleic acid molecule under siringent conditions as more fully described below.

[0049] Paralogs of a peptide can readily be identified as having some degree of significant sequence homology/identity to at least a portion of the kinase peptide, as being encoded by a gene from Drosophila, and as having similar activity or function. Two proteins will typically be considered paralogs when the amino acid sequences are typically at least about 70-75%, 80-85%, and more typically at least about 90-95% or more homologous through a given region or domain. Such paralogs will be encoded by a nucleic acid sequence that will hybridize to a kinase peptide encoding nucleic acid molecule under stringent conditions as more fully described below.

[0050] Orthologs of a kinase peptide can readily be identified as having some degree of significant sequence homology/identity to at least a portion of the kinase peptide as well as being encoded by a gene from another organism. Preferred orthologs will be isolated from mammals, preferably human, for the development of human therapeutic targets and agents, or other invertebrates, particularly insects of economical/agriculture importance, e.g. members of the Lepidopteran and Coleopteran orders, for the development of insecticides and insecticidal targets. Such orthologs will be encoded by a nucleic acid sequence that will hybridize to a kinase peptide encoding nucleic acid molecule under moderate to stringent conditions, as more fully described below, depending on the degree of relatedness of the two organisms yielding the proteins.

[0051] Non-naturally occurring variants of the kinases of the present invention can readily be generated using recombinant techniques. Such variants include, but are not limited to deletions, additions and substitutions in the amino acid sequence of the kinase. For example, one class of substitutions are conserved amino acid substitution. Such substitutions are those that substitute a given amino acid in a kinase peptide by another amino acid of like characteristics. Typically seen as conservative substitutions are the replacements, one for another, among the aliphatic amino acids Ala, Val, Leu, and Ile; interchange of the hydroxyl residues Ser and Thr; exchange of the acidic residues Asp and Glu; substitution between the amide residues Asn and Gln; exchange of the basic residues Lys and Arg; and replacements among the aromatic residues Phe, Tyr. Guidance concerning which amino acid changes are likely to be phenotypically silent are found in Bowie *et al.*, *Science 247*:1306-1310 (1990).

[0052] Variant kinases can be fully functional or can lack function in one or more activities. Fully functional variants typically contain only conservative variation or variation in non-critical residues or in non-critical regions. Functional variants can also contain substitution of similar amino acids, which result in no change or an insignificant change in function. Alternatively, such substitutions may positively or negatively affect function to some degree.

[0053] Non-functional variants typically contain one or more non-conservative amino acid substitutions, deletions, insertions, inversions, or truncation or a substitution, insertion, inversion, or deletion in a critical residue or critical region.

[0054] Amino acids that are essential for function can be identified by methods known in the art, such as site-directed mutagenesis or alanine-scanning mutagenesis (Cunningham *el al.*, *Science 244*:1081-1085 (1989)). The latter procedure introduces single alanine mutations at every residue in the molecule. The resulting mutant molecules are then tested for biological activity such as receptor binding or *in vitro* proliferative activity. Sites that are critical for binding can also be determined by structural analysis such as x-ray crystallography, nuclear magnetic resonance or photoaffinity labeling (Smith *et al.*, *J. Mol. Biol. 224*:899-904 (1992); de Vos *et al. Science 255*:306-312 (1992)). Accordingly, the protein kinases of the present invention also encompass derivatives or analogs in which a substituted amino acid resi-

due is not one encoded by the genetic code; in which a substituent group is included; in which the mature polypeptide is fused with another compound, such as a compound to increase the half-life of the polypeptide (for example, polyethylene glycol); or in which the additional amino acids are fused to the mature polypeptide, such as a leader or secretory sequence or a sequence for purification of the mature polypeptide or a pro-protein sequence.

[0055] The present invention further provides for functional, active fragments of the Chk1 kinase domain. As used herein, a fragment comprises at least 8 or more contiguous amino acid residues from the protein kinase. Such fragments can be chosen based on the ability to retain one or more of the biological activities of the kinase or could be chosen for the ability to perform a function, e.g. act as an immunogen. Particularly important fragments are catalytically activate fragments, peptides which are, for example about 8 or more amino acids in length. Such fragments will typically comprise a domain or motif of the kinase, e.g., active site or binding site. Further fragments contemplated by the present invention include, but are not limited to, domain or motif containing fragments, soluble peptide fragments, and fragments containing immunogenic structures. Predicted domains and functional sites available to those of skill in the art (e.g., by PROSITE analysis).

[0056] Polypeptides often contain amino acids other than the 20 amino acids commonly referred to as the 20 naturally-occurring amino acids. Further, many amino acids, including the terminal amino acids, may be modified by natural processes, such as processing and other post-translational modifications, or by chemical modification techniques known in the art. Common modifications that occur naturally in polypeptides are described in basic texts, detailed monographs, and the research literature, and they are known to those of skill in the art.

[0057] Known modifications include, but are not limited to, acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphotidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent crosslinks, formation of cystine, formation of pyroglutamate, formylation, gamma carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, proteolytic processing, phosphorylation, phenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. Such modifications are known to those of skill in the art and have been described in great detail in the scientific literature. Several particularly common modifications, glycosylation, lipid attachment; sulfation, gamma-carboxylation of glutamic acid residues, hydroxylation and ADP-ribosylation, for instance, are described in most basic texts, such as *Proteins - Structure and Molecular Properties*, 2nd Ed., T.E. Creighton, W. H. Freeman and Company, New York (1993). Many detailed reviews are available on this subject; such as by Wold, F., *Posttranslational Covalent Modification of Proteins*, B.C. Johnson, Ed., Academic Press, New York 1-12 (1983); Seifter *et al.* (*Meth. Enzymol. 182*: 626-646 (1990)) and Rattan *et al.* (*Ann. N.Y. Acad Sci. 663*:48-62 (1992)).

[0058] The peptides of the present invention can be attached to heterologous sequences to form chimeric or fusion proteins. Such chimeric and fission proteins comprise a peptide operatively linked to a heterologous protein having an amino acid sequence not substantially homologous to the kinase peptide. "Operatively linked" indicates that the peptide and the heterologous protein are fused in-frame. The heterologous protein can be fused to the N-terminus or C-terminus of the kinase peptide. The two peptides linked in a fusion peptide are typically derived from two independent sources, and therefore a fusion peptide comprises two linked peptides not normally found linked in nature. The two peptides may be from the same or different genome.

[0059] In some uses, the fusion protein does not affect the activity of the peptide *per se*. For example, the fusion protein can include, but is not limited to, enzymatic fusion proteins, for example beta-galactosidase fusions, yeast two-hybrid GAL fusions, poly-His fusions, MYC-tagged, HI-tagged and Ig fusions. Such fusion proteins, particularly poly-His fusions, can facilitate the purification of recombinant kinase peptide. In certain host cells (e.g., mammalian host cells), expression and/or secretion of a protein can be increased by using a heterologous signal sequence.

[0060] A chimeric or fusion protein can be produced by standard recombinant DNA techniques. For example, DNA fragments coding for the different protein sequences are ligated together in-frame in accordance with conventional techniques. In another embodiment; the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene fragments can be carried out using anchor primers which give rise to complementary overhangs between two consecutive gene fragments which can subsequently be annealed and re-amplified to generate a chimeric gene sequence (see Ausubel *et al.*, *Current Protocols in Molecular Biology*, 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (e.g., a GST protein). A kinase peptide-encoding nucleic acid can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the kinase peptide.

[0061] Herein, the term 'antibody' refers to a polypeptide or group of polypeptides which are comprised of at least one antibody combining site or binding domain, said binding domain or combining site formed from the folding of variable domains of an antibody molecule to form three dimensional binding spaces with an internal surface shape and charge distribution complementary to the features of an antigen epitope. The term encompasses immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, such as molecules that contain an antibody

combining site or paratope. Exemplary antibody molecules are intact immunoglobulin molecules, substantially intact immunoglobulin molecules and portions of an immunoglobulin molecule, including those known in the art as Fab, FabB, $F(abB)_2$ and F(v).

B. Nucleic Acids and Polynucleotides

[0062] The present invention provides isolated nucleic acid molecules that encode the functional, active kinases of the present invention. Such nucleic acid molecules will consist of, consist essentially of, or comprise a nucleotide sequence that encodes one of the kinase peptides of the present invention, an allelic variant thereof, or an ortholog or paralog thereof.

[0063] As used herein, an "isolated" nucleic acid molecule is one that is separated from other nucleic acid present in the natural source of the nucleic acid. Preferably, an "isolated" nucleic acid is free of sequences which naturally flank the nucleic acid (i.e., sequences located at the 5' and 3' ends of the nucleic acid) in the genomic DNA or cDNA of the organism from which the nucleic acid is derived. However, there can be some flanking nucleotide sequences, for example up to about 5KB, particularly contiguous peptide encoding sequences and peptide encoding sequences within the same gene but separated by introns in the genomic sequence. The important point is that the nucleic acid is isolated from remote and unimportant flanking sequences such that it can be subjected to the specific manipulations described herein such as recombinant expression, preparation of probes and primers, and other uses specific to the nucleic acid sequences.

[0064] Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques, or chemical precursors or other chemicals when chemically synthesized. However, the nucleic acid molecule can be fused to other coding or regulatory sequences and still be considered isolated.

[0065] For example, recombinant DNA molecules contained in a vector are considered isolated. Further examples of isolated DNA molecules include recombinant DNA molecules maintained in heterologous host cells or purified (partially or substantially) DNA molecules in solution. Isolated RNA molecules include *in vivo* or *in vitro* RNA transcripts of the isolated DNA molecules of the present invention. Isolated nucleic acid molecules according to the present invention further include such molecules produced synthetically.

[0066] The preferred classes of nucleic acid molecules that are comprised of the nucleotide sequences of the present are the full-length cDNA molecules and genes and genomic clones since some of the nucleic acid molecules provided in **SEQ ID NO. 1** are fragments of the complete gene that exists in nature. A brief description of how various types of these nucleic acid molecules can be readily made/isolated is provided herein.

[0067] Full-length genes may be cloned from known sequence using any one of a number of methods known in the art. For example, a method which employs XL-PCR (Perkin-Elmer, Foster City, Calif.) to amplify long pieces of DNA may be used. Other methods for obtaining full-length sequences are known in the art.

[0068] The isolated nucleic acid molecules can encode the functional, active kinase plus additional amino or carboxyl-terminal amino acids, such as those that facilitate protein trafficking, prolong or shorten protein half-life or facilitate manipulation of a protein for assay or production, among other things. The isolated nucleic acid molecules include, but are not limited to, the sequence encoding the active kinase alone or in combination with coding sequences, such as a leader or secretory sequence (eg., a pre-pro or pro-protein sequence), the sequence encoding the active kinase, with or without the additional coding sequences, plus additional non-coding sequences, for example introns and non-coding 5' and 3' sequences such as transcribed but non-translated sequences that play a role in transcription, mRNA processing (including splicing and polyadenylation signals), ribosome binding and stability of mRNA. In addition, the nucleic acid molecule may be fused to a marker sequence encoding, for example, a peptide that facilitates purification.

[0069] Isolated nucleic acid molecules can be m the form of RNA, such as mRNA, or m the form DNA, including cDNA and genomic DNA, obtained by cloning or produced by chemical synthetic techniques or by a combination thereof The nucleic acid, especially DNA, can be double-stranded or single-stranded. Single-stranded nucleic acid can be the coding strand (sense strand) or the non-coding strand (anti-sense strand).

[0070] The invention further provides nucleic acid molecules that encode functional fragments or variants of the active kinases of the present invention. Such nucleic acid molecules may be naturally occurring, such as allelic variants (same locus), paralogs (different locus), and orthologs (different organism), or may be constructed by recombinant DNA methods or by chemical synthesis. Such non-naturally occurring variants may be made by mutagenesis techniques, including those applied to nucleic acid molecules, cells, or organisms. Accordingly, as discussed above, the variants can contain nucleotide substitutions, deletions, inversions and insertions. Variation can occur in either or both the coding and non-coding regions. The variations can produce both conservative and non-conservative amino acid substitutions.

[0071] A fragment comprises a contiguous nucleotide sequence greater than 12 or more nucleotides. Further, a fragment could be at least 30, 40, 50, 100, 250 or 500 nucleotides in length. The length of the fragment will be based

on its intended use. For example, the fragment can encode epitope bearing regions of the peptide, or can be useful as DNA probes and primers. Such fragments can be isolated using the known nucleotide sequence to synthesize an oligonucleotide probe. A labeled probe can then be used to screen a cDNA library, genomic DNA library, or mRNA to isolate nucleic acid corresponding to the coding region. Further, primers can be used in PCR reactions to clone specific regions of gene.

[0072] A probe/primer typically comprises substantially a purified oligonucleotide or oligonucleolide pair. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, 20, 25, 40, 50 or more consecutive nucleotides.

[0073] Orthologs, homologs, and allelic variants can be identified using methods known in the art. As described above, these variants comprise a nucleotide sequence encoding a peptide that is typically 60-65%, 70-75%, 80-85%, and more typically at least about 90-95% or more homologous to the nucleotide sequence provided in **SEQ ID NO. 1** or a fragment of this sequence. Such nucleic acid molecules can readily be identified as being able to hybridize under moderate to stringent conditions, to the nucleotide sequence shown in **SEQ ID NO. 1** or a fragment of the sequence.

[0074] As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences encoding a peptide at least 50-55% homologous to each other typically remain hybridized to each other. The conditions can be such that sequences at least about 65%, at least about 70%, or at least about 75% or more homologous to each other typically remains hybridized to each other. Such stringent conditions are known to those skilled in the art and can be found in *Current Protocols in Molecular Biology*, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6. One example of stringent hybridization conditions are hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45C, followed by one or more washes in 0.2 X SSC, 0.1% SDS at 50-65C.

[0075] The nucleic acid molecules of the present invention are useful for probes, primers, chemical intermediates, and in biological assays. The nucleic acid molecules are useful as a hybridization probe for cDNA and genomic DNA to isolate full-length cDNA and genomic clones encoding the peptide described herein and to isolate cDNA and genomic clones that correspond to variants (alleles, orthologs, etc.) producing the same or related peptides described herein.

[0076] The nucleic acid molecules are also useful as primers for PCR to amplify any given region of a nucleic acid molecule and are useful to synthesize antisense molecules of desired length and sequence.

[0077] The nucleic acid molecules are also useful for constructing recombinant vectors. Such vectors include expression vectors that express a portion of, or all of, the peptide sequences. Vectors also include insertion vectors, used to integrate into another nucleic acid molecule sequence, such as into the cellular genome, to alter *in situ* expression of a gene and/or gene product. For example, an endogenous coding sequence can be replaced via homologous recombination with all or part of the coding region containing one or more specifically introduced mutations.

[0078] The nucleic acid molecules are also useful for expressing antigenic portions of the proteins.

[0079] The nucleic acid molecules are also useful as probes for determining the chromosomal positions of the nucleic acid molecules by means of *in situ* hybridization methods.

[0080] The nucleic acid molecules are also useful for designing ribozymes corresponding to all, or a part, of the mRNA produced from the nucleic acid molecules described herein.

[0081] The nucleic acid molecules are also useful for constructing host cells expressing a part, or all, of the nucleic acid molecules and peptides.

[0082] The nucleic acid molecules are also useful for constructing transgenic animals expressing all, or a part, of the nucleic acid molecules and peptides.

[0083] The nucleic acid molecules are also useful for making vectors that express part, or all, of the peptides.

[0084] The nucleic acid molecules are also useful as hybridization probes for determining the presence, level, form and distribution of nucleic acid expression. Accordingly, the probes can be used to detect the presence of, or to determine levels of, a specific nucleic acid molecule in cells, tissues, and in organisms. The nucleic acid whose level is determined can be DNA or RNA. Accordingly, probes corresponding to the peptides described herein can be used to assess expression and/or gene copy number in a given cell, tissue, or organism. These uses are relevant for diagnosis of disorders involving an increase or decrease in kinase protein expression relative to normal results.

[0085] *In vitro* techniques for detection of mRNA include Northern hybridizations and *in situ* hybridizations. *In vitro* techniques for detecting DNA includes Southern hybridizations and *in situ* hybridization.

[0086] Probes can be used as a part of a diagnostic test kit for identifying cells or tissues that express a kinase protein, such as by measuring a level of a receptor-encoding nucleic acid in a sample of cells from a subject e.g., mRNA or genomic DNA, or determining if a receptor gene has been mutated.

C. Vectors and Host Cells

[0087] The invention also provides vectors containing the nucleic acid molecules described herein. The term "vector" refers to a vehicle, preferably a nucleic acid molecule, that can transport the nucleic acid molecules. When the vec-

tor is a nucleic acid molecule, the nucleic acid molecules are covalently linked to the vector nucleic acid. With this aspect of the invention, the vector includes a plasmid, single or double stranded phage, a single or double stranded RNA or DNA viral vector, or artificial chromosome, such as a BAC, PAC, YAC, OR MAC. Various expression vectors can be used to express polynucleotide encoding the active hChk1 kinase.

[0088] A vector can be maintained in the host cell as an extrachromosomal element where it replicates and produces additional copies of the nucleic acid molecules. Alternatively, the vector may integrate into the host cell genome and produce additional copies of the nucleic acid molecules when the host cell replicates.

[0089] The invention provides vectors for the maintenance (cloning vectors) or vectors for expression (expression vectors) of the nucleic acid molecules. The vectors can function in prokaryotic or eukaryotic cells or in both (shuttle vectors).

[0090] Expression vectors contain cis-acting regulatory regions that are operably linked in the vector to the nucleic acid molecules such that transcription of the nucleic acid molecules is allowed in a host cell. The nucleic acid molecules can be introduced into the host cell with a separate nucleic acid molecule capable of affecting transcription. Thus, the second nucleic acid molecule may provide a trans-acting factor interacting with the cis-regulatory control region to allow transcription of the nucleic acid molecules from the vector. Alternatively, a trans-acting factor may be supplied by the host cell. Finally, a trans-acting factor can be produced from the vector itself. It is understood, however, that in some embodiments, transcription and/or translation of the nucleic acid molecules can occur in a cell-free system.

[0091] The regulatory sequence to which the nucleic acid molecules described herein can be operably linked include promoters for directing mRNA transcription. These include, but are not limited to, the left promoter from bacteriophage λ, the lac, TRP, and TAC promoters from *E. coli*, the early and late promoters from SV40, the CMV immediate early promoter, the adenovirus early and late promoters, and retrovirus long-terminal repeats.

[0092] In addition to control regions that promote transcription, expression vectors may also include regions that modulate transcription, such as repressor binding sites and enhancers. Examples include the SV40 enhancer, the cytomegalovirus immediate early enhancer, polyoma enhancer, adenovirus enhancers, and retrovirus LTR enhancers.

[0093] In addition to containing sites for transcription initiation and control, expression vectors can also contain sequences necessary for transcription termination and, in the transcribed region a ribosome binding site for translation. Other regulatory control elements for expression include initiation and termination codons as well as polyadenylation signals. The person of ordinary skill in the art would be aware of the numerous regulatory sequences that are useful in expression vectors. Such regulatory sequences are described, for example, in Sambrook et al., (*Molecular Cloning: A Laboratory Manual. 2nd ed.*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, (1989)).

[0094] A variety of expression vectors can be used to express a nucleic acid molecule. Such vectors include chromosomal, episomal, and virus-derived vectors, for example vectors derived from bacterial plasmids, from bacteriophage, from yeast episomes, from yeast chromosomal elements, including yeast artificial chromosomes, from viruses such as baculoviruses, papovaviruses such as SV40, Vaccinia viruses, adenoviruses, poxviruses, pseudorabies viruses, and retroviruses. Vectors may also be derived from combinations of these sources such as those derived from plasmid and bacteriophage genetic elements, eg. cosmids and phagemids. Appropriate cloning and expression vectors for prokaryotic and eukaryotic hosts are described in Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual. 2nd ed.*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, (1989).

[0095] The regulatory sequence may provide constitutive expression in one or more host cells (i.e. tissue specific) or may provide for inducible expression in one or more cell types such as by temperature, nutrient additive, or exogenous factor such as a hormone or other ligand. A variety of vectors providing for constitutive and inducible expression in prokaryotic and eukaryotic hosts are known to those of ordinary skill in the art.

[0096] The nucleic acid molecules can be inserted into the vector nucleic acid by well-known methodology. Generally, the DNA sequence that will ultimately be expressed is joined to an expression vector by cleaving the DNA sequence and the expression vector with one or more restriction enzymes and then ligating the fragments together. Procedures for restriction enzyme digestion and ligation are known to those of ordinary skill in the art.

[0097] The vector containing the appropriate nucleic acid molecule can be introduced into an appropriate host cell for propagation or expression using well-known techniques. Bacterial cells include, but are not limited to, *E. coli, Streptomyces, and Salmonella typhimurium*. Eukaryotic cells include, but are not limited to, yeast, insect cells such as *Drosophila*, animal cells such as COS and CHO cells, and plant cells.

[0098] As described herein, it may be desirable to express a peptide of the present invention as a fusion protein. Accordingly, the invention provides fusion vectors that allow for the production of such peptides. Fusion vectors can increase the expression of a recombinant protein, increase the solubility of the recombinant protein, and aid in the purification of the protein by acting for example as a ligand for affinity purification. A proteolytic cleavage site may be introduced at the junction of the fusion moiety so that the desired peptide can ultimately be separated from the fusion moiety. Proteolytic enzymes include, but are not limited to, factor Xa, thrombin, and enterokinase. Typical fusion expression vectors include pGEX (Smith *et al.*, *Gene 67*:31-40 (1988)), pMAL (New England Biolabs, Beverly, MA) and pRIT5 (Pharmacia, Piscataway, NJ) which fuse glutathione S-transferase (GST), maltose E binding protein, or protein A,

respectively, to the target recombinant protein. Examples of suitable inducible non-fusion *E. coli* expression vectors include pTrc (Amann *et al.*, *Gene 69*:301-315 (1988)) and pET 11d (Studier *el al., Gene Expression Technology: Methods in Enzymology 185*:60-89 (1990)).

[0099] Recombinant protein expression can be maximized in a host bacteria by providing a genetic background wherein the host cell has an impaired capacity to proteolytically cleave the recombinant protein. (Gottesman, *S., Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, California (1990) 119-128). Alternatively, the sequence of the nucleic acid molecule of interest can be altered to provide preferential codon usage for a specific host cell, for example *E. coli*. (Wada *et al.*, *Nucleic Acids Res. 20*:2111-2118 (1992)).

[0100] The nucleic acid molecules can also be expressed by expression vectors that are operative in yeast Examples of vectors for expression in yeast e.g., *S. cerevisiae* include pYepSec1 (Baldari, *et al.*, *EMBO J. 6*:229-234 (1987)), pMFa (Kurjan *et al.*, *Cell 30*:933-943(1982)), pJRY88 (Schultz *et al.*, *Gene 54*:113-123 (1987)), and pYES2 (Invitrogen Corporation, San Diego, CA).

[0101] The nucleic acid molecules can also be expressed in insect cells using, for example, baculovirus expression vectors. Baculovirus vectors available for expression of proteins in cultured insect cells (e.g., Sf 9 cells) include the pAc series (Smith *et al.*, *Mol. Cell Biol. 3*:2156-2165 (1983)) and the pVL series (Lucklow *et al.*, *Virology 170*:31-39 (1989)).

[0102] In certain embodiments of the invention, the nucleic acid molecules described herein are expressed in mammalian cells using mammalian expression vectors. Examples of mammalian expression vectors include pCDM8 (Seed, B. *Nature 329*:840(1987)) and pMT2PC (Kanfman *et al.*, *EMBO J. 6*:187-195 (1987)).

[0103] The expression vectors listed herein are provided by way of example only of the well-known vectors available to those of ordinary skill in the art that would be useful to express the nucleic acid molecules. Preferred vectors include the pET28a (Novagen, Madison, WI), pAcSG2 (Pharmingen, San Diego, CA), and pFastBac (Life Technologies, Gaithersburg. MD). The person of ordinary skill in the art would be aware of other vectors suitable for maintenance propagation or expression of the nucleic acid molecules described herein. These are found for example in Sambrook, J., Fritsh, E. F., and Maniatis, T. *Molecular Cloning*: *A Laboratory Manual. 2nd, ed, Cold Spring Harbor Laboratory*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989.

[0104] The invention also encompasses vectors in which the nucleic acid sequences described herein are cloned into the vector in reverse orientation, but operably linked to a regulatory sequence that permits transcription of antisense RNA. Thus, an antisense transcript can be produced to all, or to a portion, of the nucleic acid molecule sequences described herein, including both coding and non-coding regions. Expression of this antisense RNA is subject to each of the parameters described above in relation to expression of the sense RNA (regulatory sequences, constitutive or inducible expression, tissue-specific expression).

[0105] The invention also relates to recombinant host cells containing the vectors described herein. Host cells therefore include prokaryotic cells, lower eukaryotic cells such as yeast, other eukaryotic cells such as insect cells, and higher eukaryotic cells such as mammalian cells. Preferred host cells of the instant invention include *E. coli* and Sf9.

[0106] The recombinant host cells are prepared by introducing the vector constructs described herein into the cells by techniques readily available to the person of ordinary skill in the art. These include, but are not limited to, calcium phosphate transfection, DEAE-dextran-mediated transfection, cationic lipid-mediated transfection, electroporation, transduction, infection, lipofection, and other techniques such as those found in Sambrook, *et al.* (*Molecular Cloning: A Laboratory Manual. 2nd, ed, Cold Spring Harbor Laboratory*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989).

[0107] Host cells can contain more than one vector. Thus, different nucleotide sequences can be introduced on different vectors of the same cell. Similarly, the nucleic acid molecules can be introduced either alone or with other nucleic acid molecules that are not related to the nucleic acid molecules such as those providing trans-acting factors for expression vectors. When more than one vector is introduced into a cell, the vectors can be introduced independently, co-introduced or joined to the nucleic acid molecule vector.

[0108] In the case of bacteriophage and viral vectors, these can be introduced into cells as packaged or encapsulated virus by standard procedures for infection and transduction. Viral vectors can be replication-competent or replication-defective. In the case in which viral replication is defective, replication will occur in host cells providing functions that complement the defects.

[0109] Vectors generally include selectable markers that enable the selection of the subpopulation of cells that contain the recombinant vector constructs. The marker can be contained in the same vector that contains the nucleic acid molecules described herein or may be on a separate vector. Markers include tetracycline or ampicillin-resistance genes for prokaryotic host cells and dihydrofolate reductase or neomycin resistance for eukaryotic host cells. However, any marker that provides selection for a phenotypic trait will be effective.

[0110] While the active protein kinases can be produced in bacteria, yeast, mammalian cells, and other cells under the control of the appropriate regulatory sequences, cell- free transcription and translation systems can also be used to produce these proteins using RNA derived from the DNA constructs described herein.

[0111] Where secretion of the peptide is desired, appropriate secretion signals are incorporated into the vector. The

signal sequence can be endogenous to the peptides or heterologous to these peptides.

[0112] It is also understood that depending upon the host cell in recombinant production of the peptides described herein, the peptides can have various glycosylation patterns, depending upon the cell, or maybe non-glycosylated as when produced in bacteria In addition, the peptides may include an initial modified methionine in some cases as a result of a host-mediated process.

[0113] The recombinant host cells expressing the peptides described herein have a variety of uses. First, the cells are useful for producing a kinase protein or peptide that can be further purified to produce desired amounts of kinase protein or fragments. Thus, host cells containing expression vectors are useful for peptide production.

[0114] Host cells are also useful for conducting cell-based assays involving the kinase protein or kinase protein fragments. Thus, a recombinant host cell expressing a native kinase protein is useful for assaying compounds that stimulate or inhibit kinase protein function.

[0115] Host cells are also useful for identifying kinase protein mutants in which these functions are affected. If the mutants naturally occur and give rise to a pathology, host cells containing the mutations are useful to assay compounds that have a desired effect on the mutant kinase protein (for example, stimulating or inhibiting function) which may not be indicated by their effect on the native kinase protein.

[0116] The following examples are provided for illustration purposes.

Examples

1. Identification of the Catalytic Domain Sequence

[0117] From the complete protein sequence for the human checkpoint effector kinase (Chk1, 476 residues) available through GenBank, using sequence alignment and structures for other kinases, a homology model was devised for the kinase domain of the Chk1 protein (See **Figure 3**).

[0118] All protein kinases utilize ATP to phosphorylate their substrates, involving the transfer of a gamma phosphate to a substrate hydroxyl group. Each kinase binds ATP with its own strength, a property that is correlated by measuring K_i/IC50. The ATP molecule consists of adenine, ribose and triphosphate moieties. Each of these moieties bind to the protein in the ATP binding site (or ATP pokket). The adenine moiety always binds to the protein backbone by formation of two or three hydrogen bonds. The ribose moiety forms one to two hydrogen bonds with the protein side chains of amino acids that lay outside of the ATP pocket. The tri-phosphate moiety interacts with those catalytic amino acids of the kinase that are generally consistent across the whole protein kinase family. There is a limited specificity for each kinase within ATP binding groove. This region is referred to as the specificity pocket. Using the homology model, a schematic of the Chk1 binding site was developed, identifying the ATP binding site, the donor-acceptor-donor binding motif and the specificity pocket (See **Figure 9**). This binding site is the target for inhibitor development, e.g. the development of compounds or molecules that bind to this site to the extent that the kinase activity of the Chk1 protein is blocked or inhibited. The black and red color in **Figure 9** represents the ATP binding groove; note, Ser 147 can contribute to the binding of inhibitor. The area designated by the blue color represents the region outside of the ATP pocket that can be used for enhancement of the specificity of binding. Finally, the area in pink represents the 'specificity pocket', that region that is very different from one protein to another. This site does not contribute to the ATP binding but can be used for the design of specific inhibitors. In other words, by utilizing that region of the Chk 1 binding site that is unique to Chk1 (the specificity pocket), one may design compounds that specifically inhibit Chk1 without also inhibiting the various other kinase molecules that may not be targets of the inhibition therapy.

[0119] Analysis of the C-termini of the kinase suggested that amino acids beyond residue 265 would enhance high level expression and/or maintain the appropriate crystal structure. The homology model showed this region to be flexible, such that ending the kinase domain construct within this region can prevent the disruption of potential secondary structures. Specifically, cleaving the Chk1 protein anywhere between amino acid residues 263 and 265 would result in the destruction of helical interactions at the distal end. The homology model further predicted that the kinase segment should extend to at least residue 272 to 275 and may be further extended to residue 289-291.

[0120] In addition, including the extended region in the construct prevents the C-terminal histidine tag from interacting with the kinase domain, making it accessible for affinity chromatography. Based on these analyses, construct KH289 was designed for the expression of Chk1 kinase domain of residue 1-289 with 6xHis-tag at its C-terminus. A corresponding construct without the 6xHis-tag was also made. Two other constructs were designed based on the homology model: (1) kinase domain of residues 1-210 (KH210) and (2) kinase domain of residues 1-248 (KH248).

2. Cloning

[0121] Human Chk1 cDNA was cloned by PCR using Vent polymerase (New England Biolabs, Beverly, MA) from human thymus and testis Marathon-Ready cDNA (Clontech, Palo Alto, CA) with primers synthesized (Genset, LaJolla,

A) based on the published sequence [**SEQ ID NO. 1**] (GenBank Accession number AF1016582) [Sanchez, *Science* (1997), supra.], following the instruction from the venders. Two overlapping sequences were amplified independently, one contained the sequence of nucleotides 35-830 of **SEQ ID NO.1**, and the other contained the sequence of nucleotides 678-1480 of **SEQ ID NO.1**. These overlapping sequences cover the whole coding sequence of Chk1 plus 16 base-pairs (bps) of 3'- untranslational region. The cDNA of 35-830 encodes the kinase domain of residues 1-265.

[0122] The PCR oligonucleotide primer sequences are listed in Table 1. Restriction sites for cloning, codons for 6xHis-tag, and the stop codon were engineered in the PCR primers. Restriction site StuI preceded NcoI site which overlapped the initiation codon. SacI site followed the stop codon. When included, codons for 6xHis-tag preceded the stop codon, so that an expressed protein would have a 6xHis-tag at its C-terminus.

[0123] The amplified cDNA was cloned into expression cassette pCR-TOPO (plasmid from Invitrogen, Carlsbad, CA) following the vender's instruction and the sequences were verified by sequencing of both strands (Retrogen, San Diego, CA). The amplified cDNA sequence was identical to the sequence deposited in GenBank referenced above. The full-length Chk1 cDNA was constructed from these two overlapping cDNAs, ligating through the ClaI restriction site at 734-739. This full-length cDNA was used as PCR template to generate cDNA fragments for expression or directly to generate the full-length Chk1 expression vector. All the PCR products were cloned into pCR-TOPO for sequencing. Constructs were made for the expression of full-length Chk1 and various lengths of kinase domain with or without 6xHis-tag.

Table 1

PCR Primers*		
Primer	Sequence	SEQ ID NO.
chk6w	GAG CTC AGT ACC ATC TAT CTT TTT TGA TGT CTG G	3
KH28	GAG CTC AGT TGG TGG TGG TGG TGG TGT CCA CTG GGA GAC TCT	4
9	GAC AC	
K289	GAG CTC ATC CAC TGG GAG ACT CTG ACA C	5
Chk11	CCA TGG AGC TCA AGA AAG GGG CAA AAA GG	6
K210	GAG CTC ATT GGT CCC ATG GCA ATT CTC C	7
KH21	GAG CTC AGT GGT GGT GGT GGT GGT GGT GGT CCC ATG GCA ATT	8
0	CTC C	
K248	GAG CTC ACT CAA CTA AGA TTT TAT GCA GCA G	9
KH24	GAG CTC AGT GGT GGT GGT GGT GGT GCT CAA CTA AGA TTT TAT	10
8	GCA GCA G	

3. Chk1 Antibodies

[0124] Peptide NRVTEEAVAVKIVDMKRAVD (residues 28-47 of **SEQ ID NO. 2**) was selected for generating antibody against N-terminus of human Chk1. Peptide DDKILVDFRLSKGDGLE (residues 434-450 of **SEQ ID NO. 2**) was selected for generating antibody against C-terminus of human Chk1. Rabbit polyclonal antibodies were ordered through the Custom Antibody Production Services from Research Genetics, Inc. (Huntsville, AL). Both antibodies detected recombinant or endogenous human Chk1 as expected.

4. Fermentation

[0125] The overall scheme was follows. The 3' PCR primers were engineered to encode both untagged and tagged (with 6-histidine tag) proteins. The segment of cDNA for 1-289 was cloned into a pFastBac plasmid (obtained from Life Technologies) and an NdeI site was introduced. A recombinant baculovirus was generated using the Bacmid system (obtained from Life Technologies). The protein (KH289) was expressed in Hi-5 insect cells and purified by a combination of ion-exchange and affinity chromatography. The segments of cDNA for the full-length Chk1 (1-476AA) and the Chk1 kinase domain (1-265AA) were cloned into pAcSG2 plasmid and recombinant baculovirus was generated using BaculoGold viral DNA (obtained from Invitrogen) and a modified CellFectin transfection (obtained from Life Technologies) and plaque selection (obtained from Novagen) protocol. The expressed protein was purified using the chromatog-

raphy scheme described below. High salt concentration in buffers was found to be required to prevent precipitation of the purified proteins. The details of the protocol are discussed below.

Generation of Expression Plasmids

[0126] Plasmid pFastBac-Nde was modified from the pFastBac1 vector (Life Technologies, Gaithersburg, MD) by in vitro site-directed mutagenesis using the Muta-Gene in vitro Mutagenesis Kit (Bio-Rad, Hercules, CA) following the supplier's instruction. Two nucleotides were substituted in pFastBac1 using the following oligonucleotide:

TGA ATA ATC CGG CAT ATG TAT AGG TTT TTT **[SEQ ID NO. 14]**

This created a unique NdeI site at the original translation start site for the polyhedrin protein.

[0127] The amplified cDNA fragments were digested with the restriction enzyme StuI and SacI and cloned to plasmids pET28a (Novagen, Madison, WI), pAcSG2 (Pharmingen, San Diego, CA), or pFastBac-Nde. The pET28a vector was used for protein expression in *E.coli* and pAcSG2 and pFast-Bac-Nde were used for protein expression in insect cells. To clone the cDNA fragments encoding Chk1 kinase domain with amino acids 1-289 (construct KH289) into the pFastBac-Nde, the cDNA fragment was excised from the pCR-TOPO plasmid with restriction enzymes StuI and SacI, ligated between the blunt-ended NdeI site and SacI site. Plasmids with correct insertion were analyzed by restriction enzyme digestion. The full-length Chk1 and the kinase domain of residues 1-265 (KH265) with or without C-terminal 6xHis-tag were cloned into pAcSG2 using the restriction sites of StuI and SacI. Expression vectors for kinase domain of residues 1-210 (KH210) and kinase domain of residues of 1-248 (KH248) were made in pFastBac-Nde.

[0128] Expression in E.coli was done following the instructions supplied with the pET28a vector. Proteins expressed in the form of full-length Chk1 or kinase domain of residues 1-265 or kinase domain of residues 1-289 were in the insoluble fraction when analyzed by ReadyPreps Protein Preparation Kit (Epicentre Technologies, Madison, WI).

Generation of Recombinant Viruses

[0129] The Bac-to-Bac system (Life Technologies) was used to generate recombinant baculovirus for expression of the C-terminally 6xHis-tagged Chk1 kinase domain (amino acids 1-289, KH289) as instructed. Recombinant viruses were confirmed by PCR for the presence of Chk1 cDNA insertion. Protein expression was confirmed by SDS-PAGE or Western blot with the Chk1 polyclonal antibodies. The expression of KH289 appeared to be the highest among all the constructs. High titer stocks of recombinant viruses were generated by 2 to 3 rounds of amplification using Sf21 insect cells.

[0130] Recombinant viruses for expression of the full-length Chk1 and kinase domain of residues 1-265 were generated by co-transfection of Sf21 cells with pAcSG2 vector and BaculoGold (PharMingen, San Diego, CA).

Expression in Insect Cells

[0131] The yield of active soluble protein obtained in the *E. coli* fermentation described above was impractical for large-scale experimentation. Therefore, an alternate fermentation system was developed. Insect cells Sf9 for viral amplification, and Hi-5 cells for protein production (both from Invitrogen, Carlsbad, CA, USA) were adapted to grow in insect medium contained 1% Fetal Bovine Serum (Life Technologies, Grand Island, NY, USA). Cells were propagated and maintained in suspension culture at 27°C in either Erlenmeyer shake flask (Corning # 430183) or in an upright roller bottle (Corning Inc., Corning, NY, USA # 25290-17000) with a loosened cap for aeration. The flasks were placed in a reciprocal refrigerated shaker (Innova 4343, New Brunswick Scientific, Edison, NJ, USA) at 120 rpm. The cell density was maintained at between 5 X 10^5 to 2 X 10^6 cells/ml by diluting the cultured cell suspension with a fresh pre-warmed (27°C) medium. The viability of insect cells was maintained at 98%. The viability of insect cells were determined by microscopic count of total stained cells by trypan blue versus the total cell number in a hemocytometer.

[0132] Sf9 insect cells were used for amplification for recombinant virus stock. The recombinant baculovirus from a single plaque was pick up by a pipette tip and added to Sf9 cells monolayer in T-25 flask (Becton Dickinson Labware, Franklin Lakes, NJ, USA) with 10 ml medium SF900II and 1% of Fetal bovine Serum (Life Technologies, Grand Island, NY, USA) and incubated at 27°C. After 6 days, the culture supernatant was used as first generation of virus stock (P1) for further amplification of P2 and P3 virus stocks to 2-3 L. For large scale amplification of the P2 and P3 virus stock, P1 or P2 virus stock was added to Sf9 cells at a cell density of 1 X 10^6 cells/ml, the infection was carried out with Multiplicity Of Infection (MOI) of 0.1, cells were grown in suspension in 500ml of SF900II in 2 L roller bottle (Corning Inc., Corning, NY, USA) standing up right in a shaker incubator at 120 rpm at 27 ° C for 6 days. This process was repeated until 2-3 L viral stock (P3) were obtained. The titer of this virus stock was 1 to 5X10^8p.f.u/mL. The viral titration was determined by the plaque assay method, with serial 10-fold dilution up to 10^8 fold. The viral stock was stored at 10°C,

and used for large scale protein production within 2 months to avoid viral instability.

[0133] The Hi-5 insect cells (derived from Trichoplusia ni cells) which have been adapted to grow in medium Ex-cell 401 (JRH Biosciences, Lenexa, KS, USA) with 1% Fetal Bovine Serium were used for protein production. The cells were grown in the upright roller bottle up to cell density at 2 X 10^6 cells/ml; and were used as seed cells for bioreactor culture. The cells were grown in a 20 L stirred bioreactor with working volume at 18L (Applikon Inc., Foster City, CA, USA). Air flow rate was operated at about 10 ml per min per liter culture fluid. The air was fortified by pure oxygen in order to maintain the Dissolve Oxygen (DO_2) at 50% of air saturation. The agitation was maintained at 200 rpm throughout the cultivation. Cell density was started at about 5 X 10^5 cells/ml and cells were infected when the density reached 2 x 10^6 cells/ml. The MOI was 3 and the infection was carried out for 48 Hrs. After 48 hrs. of infection, the infected cells were harvested by centrifugation at 3,000 rpm for 10 min, at 4°C by a refrigerated centrifuge (model PR-7000M, IEC, Needham Heights, MA, USA). The cell pellets were collected and stored at -80°C.

5. Purification

6X-His tagged KH289

[0134] The basic purification scheme is depicted in **Figure 4**. Frozen cell pellets were thawed, suspended in ice-cold lysis buffer, and lyzed by microfluidizer (Microfluidics Corporation, Newton, MA). The lysis buffer contained 25 mM Tris-HCl, pH 8.0, 500 mM NaCl, 20 mM imidazole, and 14 mM __ -mercaptoethanol. The lysate was centrifuged for 40 minutes at 40,000 rpm in a Ti45 rotor in Beckman L8-70M ultracentrifuge. The soluble fraction was flowed through a 150 mL Q-Sepharose FastFlow anion exchange column (Pharmacia, Piscataway, NJ), then loaded onto a 40ml Ni-NTA agarose column (Qiagen, Santa Clarita, CA). After extensive washes with the lysis buffer, the column was eluted with 240 ml of 20 mM to 300 mM imidazole gradient in the lysis buffer. Fractions containing the Chk1 kinase domain (KH289) were identified by SDS-PAGE and pooled. The pooled fractions were dialyzed in 25 mM Tris-HCl, pH 7.5, 500 mM NaCl, 0.5 mM EDTA, and 5mM DTT overnight. The dialyzed pool was diluted with 1.5 volumes of 25 mM Tris-HCl, pH 7.5, 20 mM $MgCl_2$, 8% glycerol, 5 mM DTT and loaded immediately onto a 40 ml ATP-Sepharose column. The column was eluted with 200 ml of 25 mM Tris-HCl, pH 7.5, 500 mM NaCl, 5 mM DTT, and 5% glycerol. Fractions containing KH289 were pooled and concentrated in a Millipore Stirred Cell under 60 psi N_2 and loaded onto a 320 ml HiPrep Sephacryl gel-filtration column and eluted with the same buffer. Pooled fractions were concentrated to 7-7.5 mg/ml for crystallography or ~3 mg/ml for HTS. Protein was flash-frozen in liquid N_2 and stored at -80°C.

[0135] Maintaining salt concentration around 500 mM NaCl including 5% glycerol was found to be crucial for preventing aggregation of Chk1 proteins during purification and storage without affecting the intended use.

6X-His tagged KH265 and KH476 Chk1

[0136] Essentially the same methods were used to purify the full-length Chk1 and the kinase domain of residues 1-265 expressed in insect cells. The expression protein levels as measured after the Ni-NTA chromatography or the final yields were much lower than that of the KH289 (full length sequence).

[0137] Gel-filtration HPLC has been used as a means of quality control. No significant difference was observed for samples stored at room temperature, 4°C, or -80°C for 4 days. The material eluted at a void volume that was less than 0. 1%.

6. Crystallization, Crystallography and Three-Dimensional Analysis

[0138] The full length Chk1 protein (1-476 AA) had proven to be difficult to crystallize until the active kinase domain (1-289 AA) was identified. This active kinase was able to be expressed at the high concentration required for use in HTS and crystallography. The Chk1 data set was collected on MarIP345 under cryotemperature with stream freeze. The HB2-092 kinase domain preparation (1-289 AA) was first used. The initial data set at 2.35 ◯ was obtained with overall Rsym of 4.6% and overall mosaicity for the data set is 1.2. Subsequent experiments with the HB2-101 (also a 1-289 clone) reached a 1.7 ◯ resolution with mosaicity of 0.38 for the kinase domain using a crystal grown in refined conditions. Both the original and subsequent crystals have a space group P21 with one molecule per asymmetric unit. The results from the crystallographic analysis are shown in Table 2 below.

Table 2: Statistics for the crystallographic analysis

Crystal	Nat1	Nat2	AMP-PNP	Hg	Au
Internal merging and scaling					
Resolution (Å)	1.7	2.1	1.7	2.4	2.0
Reflections measured	162418	46947	107449	64881	125728
Unique reflection	35032	19145	35285	12821	22086
Completeness (%)	93.6 (88.3)	95.4(94.6)	94.1 (91.1)	95.4 (96.4)	97.5 (84.8)
Average I/σ	29.9 (9.0)	15.47(4.38)	26.4 (12.5)	27.1 (11.6)	33.5(14.8)
R_{sym}[1]	3.2 (18.1)	5.0(23.3)	3.0 (10.0)	6.0 (13.2)	4.2 (11.8)
SIRSAS analysis					
Resolution (Å)				15-3.0	15-3.0
Rcullis[2]				0.49	0.55
Phasing power[3] (SIR/SAS)				2.27/1.98	2.39/1.48
Figure of merit (combined)					0.764
Refinement statistics					
Resolution range (Å)	7-1.7	7-2.1	7-1.7		
Reflections used[4] (F>1σF)	30132	15804	31794		
Total nonhydrogen atoms	2372	2354	2460		
Rcryst[5] (%)	21.6	20.8	22.6		
Rfree[6] (%)	23.5	25.0	24.9		
rmsd from ideal bond length (Å)	0.005	0.006	0.010		
rmsd from ideal bond angle (°)	1.30	1.27	1.58		
Average B (Å^2 ; all atoms)	28.9	29.7	23.22		

Data for the outermost resolution shell are given in parentheses.

1 $R_{sym} = \sum_{h} \sum_{i=1}^{N} |I(h)-I(h)_i| / \sum_{h} \sum_{i=1}^{N} I(h)_i * 100$,

where $I(h)_i$ is the ith measurement of reflection h and I (h) is the mean value of the N equivalent reflections.

2 Rcullis = • | | FPH +/- FP | - FH(calc) | / • | FPH +/- FP | for all centric reflections.

3 Phasing power = r.m.s. (| FH | / E), where | FH | is the heavy-atom structure factor amplitude and E is the residual lack of closure.

4 Number of reflections used in working set.

5 Rcryst = • | |Fobs| - | |Fcalc| |/•|Fobs|, where summation is over data used in the refinement.

6 Rfree is the same calculation including the 10% of data excluded from all refinements.

[0139] Crystals were grown at 13°C using a hanging-drop vapor-diffusion method. Two crystallization conditions produced the exact same form of crystals. The Nat1 crystal was obtained by mixing equal volume of protein solution (7- to 7.5 mg/ml protein) and reservoir solution of 13% PEG 8000 (w/v), 0.115 M $(NH_4)_2SO_4$ 0.1 M NaCacodylate (pH 6.8), 2% glycerol. The Nat2 crystal was crystallized using reservoir solution of 12% PEG8000 (w/v), 15% isopropanol, 0.1 M Hepes (pH 7.5). The crystals belong to the space group $P2_1$ and have unit cell dimensions a = 45.2Å, b = 65.7Å, c = 58.1Å, d = 93.9°. The crystals contained one molecule per asymmetric unit and are 53% solvent by volume. The crystals of binary complex with AMP-PNP were obtained by co-crystallization first under the same crystallization condition as Nat1 crystal in the presence of 1.25 mM AMP-PNP and 2.5 mM $MgCl_2$, then the resulting crystals were soaked in mother liquor containing 5 mM $MgCl_2$ and 20 mM AMP-PNP for two days. The co-crystals had the identical space group ($P2_1$) and cell dimensions as the native crystals. All diffraction data were collected at -170°C. Crystals were introduced into cryoprotectant solution containing its reservoir solution and 20% glycerol. For AMP-PNP co-crystal, additional 10 mM $MgCl_2$ and AMP-PNP were included in cryoprotectant solution. Crystals were then flash frozen in a stream of nitrogen gas -170°C. All data collection was carried out with home source using CuK γ-radiation produced by a Rigalu rotation anode FR5 X-ray generator equipped with focusing mirrors and measured with a Mar 345 image-plate detector. All data were processed with the Denzo/HKL package (Otwinowski, Z., "Oscillation Data Reduction Program", *Proceedings of the CCP4 Study Weekend: Data Collection and Processing*, pp. 56—62, compiled by: L. Sawyer, et al., SERC Daresbury Laboratory, England (January 29-30, 1993)).

[0140] Initial apoenzyme structure determination using Nat1 crystal data was carried out by molecular replacement (MR) using modified Cdk2 structure (omitted loop regions) (Russo, AA et al., *Nature* **382**(6589):325-31 (Jul 25, 1996)) as a search model. Rotation and translation functions using the AMoRe software (Navaza J, *Acta Crystallographic*, **50**(2): Section A (March, 1994)) revealed a solution using Nat1 data from 10 to 4 Å. The MR model was refined by simulated annealing (X-plor). However, after successive rounds of rebuilding and refinement, 2Fo-Fc and Fo-Fc electron density maps were poorly defined at the loop regions which were omitted from the initial model. To obtain additional phase information, multiple isomorphous replacement was carried out with two heavy metal derivatives: 0.5 mM $HgCl_2$ (soaked for 15 hrs) and 5 mM Kau $(CN)_2$ (soaked for 17 hrs). Five Hg sites and five Au sites were identified by difference Fourier synthesis using phases generated from the MR partial model and were consistent with both isomorphous and anomalous difference Patterson maps. The positional and thermal parameters and relative occupancies for the heavy atom sites were refined using SIR data at 3 Å and anomalous data at 3.5 Å by program PHASES (Furey, W et al. "Phases: a Package of Computer Programs Designed to Compute Phase Angles for Diffraction Data from Macromolecular Crystals", *American Crystallographic Association*, Series 2, **18**:73 (1990)). Sixteen cycles of solvent flattening were then carried out using phases calculated from refined Hg and Au positions. The resultant electron density maps showed a good backbone density and well-defined side chains for most part of the protein. Model building utilized the program FRODO (Jones, T.A., *J Appl Cryst*, **11**: 268-272 (1978)). The missing loop regions were incorporated into the model using both MIR maps and model phased 2Fo-Fc maps. Further refinement in XPLOR (Brünger, A.T. et al., X-PLOR Version 3.1: A System for X-ray Crystallography and NMR", Yale University Press, (1992)) and then CNS (Brünger, A.T. et al, Crystallography & NMR System, *Acta Cryst.*, **D54**: 905-921 (1998)) were continued with both conjugate gradient minimization and simulated annealing, then followed by manually rebuilding.

[0141] Refinement of Nat2 structure was carried out by using refined Nat1 model but omitting residues 153-170 as well as SO_4. Fo-Fc maps showed well defined densities for the omitting region and its conformation is exactly same as that in Nat1.

[0142] Refinement of the binary complex with AMP-PNP was proceeded with refining the position of the refined apo-enzyme model (Nat1) as rigid body against the complex data using CNS program. Fo-Fc maps with $\_A$ (Read, R.J., *Acta Cryst.*, **A42**: 140-149 (1986)) weighting showed clear density for the adenine and ribose components of AMP-PNP. The conformation of residues forming the binding pocket was checked in simulated annealing omit maps before including the adenine and ribose components of AMP-PNP.

[0143] The apo-enzyme model (Nat1) included all atoms for residues 2 to 44 and 48 to 276, 183 ordered solvent molecules and one SO_4 molecule. The refined Nat2 structure contained the same number of residues and solvent molecules but the SO_4 molecule was not present. The refined AMP-PNP complex contained the same number of residues as apo-structures, with 150 ordered solvent molecules and one SO_4 molecule. The triphosphate moiety of AMP-PNP was disordered and no Mg^{2+} ions were visible. The final model had all residues in "most favored" or "additional allowed" regions of the Ramachandran plot according to PROCHECK (Laskowski RA et al., *J. Appl. Cryst.*, **26**: 283-291 (1993)), with no residues in "generously allowed" or "disallowed" REGIONS, indicating the well refined nature of the identified crystal structure. The terms "generously allowed" and "disallowed" are descriptions of the configuration of Phi and Psi angles of the protein structure. A well refined protein structure should not place these angles in the unpreferred or non-naturally occurring configurations.

7. The Overall Kinase Structure

[0144] The crystal structures of the kinase domain of human Chk1 and its binary complex with an ATP analog, AMP-PNP, have been determined to 1.7 Å resolution. Both structures contain the kinase core domain (residues 2-267) and residues in the linker region that connects the N-terminal kinase domain with the C-terminal region of Chk1. The crystallographic analysis is summarized in **Table 2**. The Chk1 crystal coordinates for the apoenzyme (isolated active Chk1) and the binary complex (Chk1 complexed with AMP-PNP, an ATP analog) are shown in Figures 11A and 11B, respectively. The coordinates of the fixed water molecules are also included therein.

[0145] The kinase domain of human Chk1 has a canonical kinase two-lobe fold, with the ATP binding cleft between the two lobes (**Figure 5**, *structure model*). The smaller N-terminal lobe contains one helix (αC) and 5 β-strands (β1 to β5) that form a curved anti-parallel β-sheet. The larger C-terminal lobe contains a cluster of 7 helices (αD to αI), packed against 6 β strands (β6 to β11) which border the cleft. One β strand (β6') comprises the hinge region connecting the two lobes. In both apo-enzyme and binary structures, the ATP binding site, catalytic residues, and the activation loop are well ordered. Comparison with crystal structures of other kinases indicates that the Chk1 kinase domain is closely related to PhK (Lowe, ED et al., *EMBO J*, **16**(22):6646-58 (Nov 17, 1997)) (See **Figure 1A, 1B**). The N-terminal lobe (Residues 2-90) superimposes with an r.m.s. derivation for Cα atoms of 1.1 Å, while the C-terminal lobe (Residues 91-276) superimposes with an r.m.s. derivation for Cα atoms of 0.9 Å. In the C-terminal lobe, major differences are found in helix αG, and the connecting loop between αG and αH. These are not included in the superposition. The Chk1 apoenzyme adopts a more open conformation compared to PhK. The N-terminal lobe of Chk1 is rotated ~15° relative

to the ternary complex of PhK with its substrates. Comparison of the AMP-PNP bound Chk1 binary complex with the apoenzyme structure shows no conformational change. A high degree of sequence homology for Chk1 kinase domains of different species (**Figure 2**) suggests that there is an overall structural conservation of the kinase domain. Residues that are not modeled in the current structures are not conserved in Chk1. For example, there is a six-residue insertion in the loop connecting β3 and αC in S. pombe Chk1.

[0146] The two lobes are held together by an extensive hydrogen-bond network at the lobe interface which involves the loop linking αC and β4 of the N-terminal lobe, β6' of the hinge region, and β7 and β8 of the C-terminal lobe. This network extends from the back of the protein to the front opening of the ATP binding cleft. Residues involved in this network also form part of the pocket that interacts with the adenine moiety of AMP-PNP. Strand β8 immediately precedes the kinase conserved DFG motif, in which Asp148 is important for the alignment of the phosphate groups of ATP. The only reported mutation in the Chk1 kinase domain is at the lobe interface. Replacement of the conserved Glu85 by Asp leads to a temperature-sensitive phenotype in fission yeast in which the mutant maintains cell cycle arrest after UV irradiation but impairs the DNA replication checkpoint at nonpermissive temperature (Francesconi, S et al., *EMBO J*, **16**(6):1332-41 (Mar 17, 1997)). The side chain of Glu85 at the end of strand β5 forms hydrogen bonds with the side chain of conserved Lys145 from strand β8 as well as with the main chain amide of conserved Lys69 that precedes strand β4. These interactions, together with the extensive hydrogen-bond network at the lobe interface, appear to play an important role in maintaining the correct disposition of the N-terminal lobe and the DFG loop during lobe movement. The Glu to Asp mutation, while maintaining similar charge, would not be long enough to form those hydrogen bonds provided by Glu85, thereby weakening lobe interactions and rendering the mutant protein less stable at higher temperature.

[0147] Most of the invariant residues of Chk1 proteins are located in the C-terminal lobe. Many of them are also conserved among Ser/Thr kinases and are involved in stabilizing the catalytically active kinase conformation and in binding ATP. The positions of several invariant motifs of Chk1 proteins are noteworthy. Compared with other Ser/Thr kinases, the IEPDIG motif (residues 96-101) shortens αD to a one-turn helix, since Pro98 initiates a tight turn between αD and αE. This turn interacts with the C-terminus of helix αF through a backbone hydrogen bond between Asp99 and the invariant Gly204. In this turn, Glu97 forms backbone hydrogen bonds with Ile100 and Gly101. The unique conformation of this motif appears to be important for peptide substrate interaction, since the side chains of Ile96 and Pro98 form part of a hydrophobic pocket that interact with the peptide substrate as discussed below. Helix αE contains a conserved motif of AQXFFXQL (residues 107-114; SEQ ID NO: 24), with the hydrophobic residues buried inside the C-terminal lobe. The side chain of Gln108 projects towards the linker region that follows the kinases core domain and forms hydrogen bonds directly or through a water molecule to backbone atoms of Lys267, Leu269 and Lys270. Although Chk1 sequences diverge in this linker region, these backbone interactions with Gln 108 could still be conserved, holding the linker against the N-terminus of αE. Helix αG is positioned differently compared with αG of PhK. Two sets of invariant PW residues (207 and 208, 230 and 231) flanking αG, although separated by 21 residues, are in van der Waals contact and connected to the hydrophobic core of the C-terminal lobe. This stabilizes the surface for peptide substrate interaction.

Activation and Catalytic Loops

[0148] Interesting features of the Chk1 kinase domain include interactions that stabilize the activation loop. The structure of the activation loop determines the alignment of residues contacting ATP and performing catalysis in protein kinases. Interacting with the catalytic loop, the activation loop orients the catalytic Asp; interacting with the N-terminal lobe, the activation loop closes the N and C terminal lobes and aligns residues that interact with the phosphates of ATP. The activation loop is defined as the region between the conserved motifs of DFG and APE corresponding to residues 148 to 177 of Chk1. Conformational changes in the activation loop serve as a major regulatory mechanism for kinase activity. In the human Chk1 structures, the activation loop is folded in a conformation similar to those found in structures of active kinases, consistent with the observation that the Chk1 kinase domain is constitutively active. This active conformation is stabilized by special features of Chk1 secondary structures and their side chain interactions (**Figures 3 and 5**, *homology model and crystal structure*).

[0149] The N-terminus of the activation loop interacts with the catalytic loop through the interaction of β6 and β9. Immediately following β9, β10 interacts with β11 to form a two-stranded β-loop with a turn at Asn159. This β-loop is packed against the N-terminus of the catalytic loop and positions the highly conserved Arg156 and Glu161. The side chain of Arg156 interacts with the carbonyl of the invariant His122 at the end of αE. Through the invariant Asp190, the side chain of His122 is connected to the amide of Arg129, adjacent to the catalytic residue Asp130. The carboxyl of Glu161 forms a hydrogen bond with the imidazole of His185 that precedes αF. These interactions anchor this end of the activation loop to the core of the C-terminal lobe. The center of the activation loop interacts with the rest of C-terminal lobe through two backbone hydrogen bonds between Leu164 and Phe184. The activation loop ends at its C-terminus with a turn which is supported by αEF. In human Chk1, αEF is anchored at two positions to the core of the C-terminal

lobe through two ion-pairs, one is the invariant kinase ion-pair between Glu177 and Arg253, another is between Lys180 and Glu248 which is unique to Chk1. This extra ion-pair constrains the movement of αEF, and in turn the movement of the C-terminal end of the activation loop. The pair of Lys180 and Glu248 is only conserved in vertebrate Chk1, suggesting potential flexibility of αEF and the activation loop of Chk1 in lower organisms such as S. pombe.

[0150] Crystal structures of kinases indicate that the conformation of the activation loop is influenced by its negative charge which neutralizes a cluster of positively charged residues, although the ionic interaction may not be absolutely required as in the case of mammalian casein kinase I. The negative charge is provided by phosphate through phosphorylation, carboxyl group of Glu, or solvent ions. In Chk1, the positively charged cluster of Arg129, Arg162, Lys166, and Lys54 is present, but no phosphorylation is observed. In both the apoenzyme and binary complex structures determined to 1.7 Å, a sulfate ion was close to the phosphate position of the phosphothreonine (Thr197) in PKA. This sulfate ion interacts with Arg129, Arg162, and Thr153. Sulfate is present in the crystallization solution and could contribute to the stability of the positively charged cluster and the activation loop. To clarify the role of this sulfate ion and to better understand the interactions that stabilize the activation loop, crystals were produced under sulfate-free condition and determined the structure to 2.1 Å (**Table 2**). This 2.1 Å structure is referred as Nat2 structure, whereas the 1.7 Å apoenzyme structure is referred as Nat1 structure. In Nat2 structure, no sulfate ion is present.

[0151] Superimposition of Nat1 and Nat2 structures revealed similar conformations for the corresponding activation loops except for the side chain of Arg162 which turns toward the solvent in Nat2 structure. The side chain of Arg162 is flexible in both structures as indicated by its high temperature factors. Arg162 is an invariant residue of Chk1 and its function is not readily apparent from the structure. In both the Nat1 and Nat2 structures, the side chain of Arg129 forms hydrogen bonds to three main chain carbonyl oxygens (Leu151, Ala152, and Lys166) directly or via water molecules. The positive charge of Arg129 could be neutralized by the thiol group of Cys168 which is in the vicinity of side chains of Lys166 and Arg129. In this basic environment, this thiol could become a thiolate ion. Cys168 is invariant in Chk1 and is conserved in many kinases such as PKA and PhK. Our results rule out the role of sulfate ion in stabilization of the activation loop of Chk1. Instead, the activation loop and the catalytic loop are stabilized by its unique secondary structures and their extensive side chain interactions.

[0152] A difference between Chk1 and other kinases is the permuted positions of Lys166 and Thr153 (**Figure 2**). Lys166 occupies the equivalent position as Glu182 of PhK and the phosphorylated Thr197 of PKA, whereas Thr153 is equivalent to Lys189 of PKA. The side chain of Thr153 forms a hydrogen bond with the side chain of Lys54 located in helix αC. Thr153 is conserved in Chk1 (Thr or Ser) and is a candidate for phosphorylation in the activation loop. The permuted position, however, makes phosphorylation of Thr153 unlikely. The activation loop is already in an active conformation in Chk1 and phosphorylation would be unnecessary. Lys54 is conserved in all but S. pombe Chk1 and adjacent to Glu55 which forms the invariant ion-pair with Lys38 in active kinases. The interaction between Thr153 and Lys54, therefore, appears to play a similar role to the interaction between His87 and the phosphate of Thr197 of PKA. The side chain of Lys166 points to Cys168 and its position appears to play a role in determining the substrate specificity as discussed below. In *S. pombe* Chk1, the residue that corresponds with Lys166 is Ser, suggesting potential regulation of the activity of *S. pombe* Chk1 through phosphorylation. Concomitantly, the activation loop of *S. pombe* Chk1 appears to be more flexible since its substitutions would disrupt some of the interactions that stabilize the activation loop.

Catalytic Residues and AMP-PNP Binding

[0153] The glycine-rich loop that anchors the phosphate groups of ATP in kinases is poorly ordered in Chk1, as evidenced by the high B factors in this region for both apoenzyme structures and AMP-PNP bound binary complex structure. Residues 18-21 at the apex of the loop between β1 and β2 are flexible with poor electron density. These residues are highly conserved in kinases and anchor the β-phosphate of ATP in ATP-bound kinase structures. The flexibility of this loop could play a role in regulating Chk1 kinase activity, indeed, Tyr20 present in higher organisms corresponds structurally to Tyr15 of Cdc2 which following phosphorylation inhibits Cdc2 activity (Coleman TR, et al., *Curr Opin Cell Bio*, **6**(6):877-82 (Dec, 1994); Russo, AA et al., *Nature*, (1996), supra).

[0154] One striking feature among the active ternary complexes such as PKA and PhK is the close similarity of the active site residue conformation, their interactions with the ATP and coordination of the metal ions. The binary complexes that have been solved show no such conservation (Knighton DR, et al., *J Mol Biol*, **220**(2):217-20 (Jul 20, 1991); Bossemeyer, D et al., *EMBO J*, **12**(3): 849-59 (Mar 1993); Zheng J, et al., *Protein Sci*, 2(10):1559-73 (Oct 1993); Owen DJ, et al., *Structure*, **3**(5):467-82 (May 15, 1995); Lowe, et al., *EMBO J*, (Nov 17, 1997), supra.). Many of the active site residues in the Chk1 structure have interactions quite similar to those in ternary complexes of Phk and PKA (**Figure 4A, 4B**). In the N-terminal lobe, the invariant ion pair of active kinases is present between Lys38 and Glu55; the corresponding Lys in PhK and PKA interacts with α and β phosphates of ATP. Helix αC is firmly attached to the rest of N-terminal lobe through hydrophobic interactions and is in an active position relative to the rest of the N-terminal lobe. It also interacts with the DFG loop in the C-terminal lobe, the side chain of Glu55 from αC rests above Gly150. The relative side chain positions of Lys38, Glu55, and Asp148 are similar to those for the corresponding residues in the ternary com-

plexes of PKA and PhK. These residues in PKA and PhK, together with the glycine-rich loop, coordinate a Mg^{2+} and anchor the α and β phosphates of ATP. In the C-terminal lobe, the conformation of the catalytic loop (residues 130-135) of Chk1 is nearly identical to that in PhK with the side chains of Asp130, Lys132, and Asn135 in Chk1 nearly superimposable to the corresponding residues Asp149, Lys151, and Asn 154 in PhK in which Lys151 binds to the γ-phosphate of AMP-PNP and Asn154 chelates another Mg^{2+} that binds to the β and γ phosphates of AMP-PNP. Thr170 is conserved in all serine/threonine protein kinases and appears to determine the specificity of Ser/Thr verses Tyr as phospho-acceptor. Thr170 forms hydrogen bonds with Asp130 and Lys132 analogous to Thr186 in PhK and these interactions are needed for the positioning the carbonyl of the catalytic residue Asp130. The residues of Chk1, however, are far apart from those in the N-terminal lobe and the DFG loop due to the somewhat open lobe conformation (**Figure 6**). The DFG loop is positioned higher than its counter parts in PKA and PhK. Lys38Nε is 10 Å away from Asp130Oδ2, compared with 8.2 Å in Phk and 7.8 Å in PKA. Asp148Oδ1 is 6 Å away from Asp130Oδ2, compared with 3.8 Å in PhK and 4.8 Å in PKA. In Chk1, one water molecule is located between Asp148 and Asp130 and is hydrogen bonded to Asp130Oδ2 as well as Asn135Oδ1. The side chain of Asn135 is over 1 Å farther away from Asp148 relative to the active conformation in PhK. The residues that are necessary for ATP phosphate binding and catalysis are clustered in two separate parts, although they maintain their local interactions. The lack of electron density of the triphosphate moiety of AMP-PNP in the binary complex of Chk1 probably results from misalignment of these residues as well as flexibility in the glycine-rich loop.

[0155] The adenine and ribose moieties are clearly defined in our current model. As in all the structures of kinases with ATP, the adenine base is almost completely buried in a hydrophobic pocket between the two lobes, and hydrogen bonds are formed between N6 of adenine and the main chain carbonyl of Glu85, and between N1 and amide of Cys87. As in PhK, Chk1 N7 interacts with the side chain of Ser147 via a water molecule in Chk1. However, the ribose ring adopts a C2'-*endo* conformation similar to that in the inactive form of Cdk2 (PDB ID code 1HCK, (De Bondt HL, et al., *Nature*, **363**(6430):595-602 (Jun 17 1993); Schulze-Gahmen U et al., *J Med Chem*, **39**(23):4540-6 (Nov 8, 1996)), with the O2' hydrogen-bonding to Glu91, and O3' hydrogen bonding to the carbonyl of Leu15 in the glycine-rich loop. In comparison, the ribose rings have C3'-*endo* puckering in the active ternary complexes of PKA and PhK.

Substrate Specificity and Interactions That Stabilize the Closed Conformation

[0156] The structured activation loop of Chk1 provided an opportunity to explore the basis of peptide substrate specificity. The close resemblance of Chk1 with PhK and the available structures of PhK with and without peptide substrate enable us to model the interactions of peptide substrate with Chk1. The interaction of kinases with their peptide substrates has been analyzed for three kinases, PKA with an inhibitor peptide of PKI (PDB code 1ATP, (Knighton DR. *J Mol Biol*, (Jul 20, 1991); supra.), PhK with MC-peptide (PDB code 2PHK, (Lowe, et al., *EMBO J*, (Nov 17, 1997), supra.), and insulin receptor tyrosine kinase with a peptide substrate (PDB code 1IR3, (Hubbard SR, *EMBO J*, **16**(18):5572-81(Sep 15, 1997)). In all three tertiary complex structures, the backbones of peptide substrates around the phosphate acceptor residues adopt extended conformation and interact mainly with the C-terminal lobes.

[0157] The known Chk1 kinase substrate is the Cdc25C protein phosphatase. Several phosphate acceptor Ser residues have been identified in the Cdc25C protein sequence. Consensus features can be derived from sequences surrounding the phosphate acceptor Ser (position P): The N-terminal P-3 position is a conserved Arg, P-5 positions prefers bulky hydrophobic residues, and P-2 is Ser or Thr. Phosphorylation of Ser216 of human Cdc25C is required for DNA damage induced G2 arrest and Ser216 is phosphorylated by Chk1 in vitro (Peng et al., *Science* (1997), supra.; Sanchez et al., *Science* (1997), supra.). Therefore, the peptide LYRSPSMPE spanning residues 211-219 of human Cdc25C was used to model the interaction of peptide substrate with Chk1, based on the ternary complex of PhK with MC-peptide.

[0158] The modeled Cdc25C peptide easily fits into a groove on the C-terminal lobe of Chk1, following a path very similar to that of the MC-peptide bound to PhK (**Figure 7**). The Oγ atom of Ser(P), the presumed nucleophile in the phosphate transfer reaction, is very close to an ordered water molecule in Chk1 structures. This water molecule hydrogen bonds to both the Asp130Oδ2 and Lys132Nε. Superposition of Chk1 and PhK shows that this water molecule would be 3.4 Å from the γ-phosphorus atom of the AMP-PNP in PhK. The position of this water molecule probably indicates the approximate location of the seryl hydroxyl during catalysis.

[0159] The hydrophobic side chain of Leu(P-5) fits into the hydrophobic pocket formed by Phe93, Ile96, Pro98, and Leu206. All of these residues except Leu206 are invariant in Chk1 proteins. The side chain of Arg(P-3) points towards Glu91 of Chk1. However, in its extended conformation, the guanidinium group of this Arg can only make a hydrogen bond (3 Å) with the carboxyl of Glu91. In both PKA and PhK, the guanidinium of Arg(P-3) forms a salt bridge (2.5 Å) with the carboxyl of the corresponding Glu residues. As discussed below, ionic interaction of Arg and Glu91 could be established after lobe closure.

[0160] The side chain of Ser(P-2) could make a hydrogen bond to the backbone carbonyl oxygen of Pro(P-1). In PhK, Gln(P-2) of the MC-peptide interacts with Ser188. This interaction is not available to Chk1 since it has an invariant

Pro172 in the corresponding position of Ser188 in PhK. Pro172, then, may contribute to the specificity of Chk1 for Ser or Thr at P-2 position and the internal hydrogen bond provided by Ser or Thr at P-2 position may play a role in maintaining the conformation of the substrate backbone at its N-terminus.

[0161] The hydrophobic side chain of Met(P+1) projects into a hydrophobic pocket formed by residues of Leu171, Val174, Leu178, Leu179, and Met167. The P+2 position can only accommodate a small side chain or a turn due to the unique position of Lys166. Lys166 is conserved among vertebrate Chk1 proteins. Correspondingly, Pro is found at the P+2 position of the Cdc25 substrates. Pro(P+2) creates a consensus 14-3-3 binding site once the Ser(P) is phosphorylated. The Lys166 of human Chk1 is a Ser residue in S. pombe Chk1. The side chain of S. pombe Chk1 could be phosphorylated and point to the position corresponding to the sulfate ion in human Chk1 structure. Correspondingly, bulky side chains are present at the P+2 position of the substrates of S. pombe Chk1.

[0162] Phosphorylation of Cdc25C by Chk1 is very specific such that the Ser(P-2) is not phosphorylated. This is important for Cdc25C regulation since phosphorylation at the P-2 position would destroy the 14-3-3 binding site. Our model clearly indicates determinants for Chk1 substrate specificity: hydrophobic interaction through the P-5 and P+1, ionic interaction through P-3, Ser/Thr at P-2, and small amino acid side chains at the P+2 position.

[0163] Although the recombinant Chk1 kinase domain is active when assayed in solution, the structure reveals that it is not in a closed catalytically active conformation in either the apoenzyme or the binary crystal structure. This result suggests that the apoenzyme and the ATP bound binary complex favor the open conformation. Lobe movement is common in kinase domains and catalysis requires a closed conformation (Cox S, et al., *Curr Opin Struct Biol*, **4**(6):893-901(Dec, 1994); Gangal M, et al., *Biochemistry*, **37**(39):13728-35 (Sep 29, 1998)). Interactions that stabilize the closed active conformation have not been addressed in detail in previous reports. Our model suggests that a key interaction in Chk1 is the ion-pair between Glu91 with Arg(P-3) of peptide substrate.

[0164] Superposition of Chk1 and PhK structures indicates that lobe closure of Chk1 can be achieved by a simple rotation of the N-terminal lobe by ~15 degree around residue Glu91. This rotation would place Glu91 closer to Arg(P-3) and establish an ion-pair between the carboxylate group of Glu91 and the guanidinium group of the Arg(P-3). Lobe closure could also change the ribose conformation of AMP-PNP to a C3'-*endo* conformation from the C2'-endo conformation in the binary complex. The catalytically active kinase ternary complex structures reported to date have their respective ribose rings puckered in a C3'-*endo* conformation. For Chk1, when the ribose is modeled in a C3'-*endo* conformation, two hydrogen bonds can form between the carboxyl group of Glu91 and the O2' and O3' of the ribose. In comparison, the binary complex of Chk1 with AMP-PNP has only one hydrogen bond between Glu91 and the ribose. The Chk1 kinase domain in solution likely shifts dynamically ("breathes") between the open and closed conformation. The current Chk1 structures have open conformations and have revealed that the ATP binding cleft is accessible to solution. In the closed conformation, residues for phosphate binding and catalysis come together and align the phosphate for transfer. The additional interaction of Glu91 with Arg(P-3) of peptide substrate and with the ribose of ATP would shift the equilibrium to the closed active conformation. Therefore, peptide substrates gain specificity partly through their ability to stabilize the closed catalytically active conformation of Chk1.

8. Regulation of Chk1 Kinase Activity

[0165] Phosphorylation of the Chk1 substrate, Cdc25, and the resulting cell cycle arrest has been correlated with the activation of Chk1 after DNA damage. Whether phosphorylation of Chk1 regulates its kinase activity is unclear. The structure of human Chk1 suggests that its activity is not regulated through phosphorylation of the activation loop. Instead, the activation loop of Chk1 appears to be anchored by extensive interactions through rigid secondary structures and their side chains. Interestingly, phosphorylation of the activation loop could occur in S. pombe Chk1 which has a Ser substitution at the position of Lys166. Whether Chk1 is regulated differently in S. pombe and mammals requires the identification of residues that are phosphorylated after DNA damage.

[0166] The structure of the Chk1 kinase domain and its binary complex with AMP-PNP provide insight into its activation mechanism. First, the structures reveal an unique arrangement of the residues for phosphate binding and catalysis. Specifically, the residues for α and β phosphate binding are separated from those for γ phosphate binding and catalysis. Alignment of these residues is achieved in a closed conformation which is stabilized by peptide substrate. Our model predicts low ATPase activity of Chk1 and favors an ordered kinetic mechanism in which ATP binding precedes the peptide substrate binding. Secondly, the structures exclude a role for the activation loop of human Chk1 in regulating the kinase domain conformation. The activation loop is most likely maintained by rigid secondary structures and the extensive interactions of their side chains. However, a possibility of different regulatory mechanism exists for S. pombe Chk1, which may reflect their different cell cycle processes and different DNA damage repair mechanisms. In addition, the interactions that stabilize the active kinase conformation have been identified. The presence of Glu in many kinase hinge regions and Arg at P-3 position of their substrates suggests a general role for this interaction in maintaining the closed conformation for Ser/Thr kinases. Interactions that determine the peptide substrate specificity suggest a consensus sequence that is useful to identify potential Chk1 substrate. Finally, Chk1 kinase domain structure provides a guide

for its future characterization as well as design of specific inhibitors that could abrogate checkpoint control for cancer therapy.

9. Enzymatic Activity of Chk1

[0167] The enzymatic activity of a kinase is measured by its ability to catalyze the transfer of a phosphate residue from a nucleoside triphosphate to an amino acid side chain in a selected protein target. The conversion of ATP to ADP generally accompanies the catalytic reaction. Herein, a synthetic substrate peptide, Syntide-2, having amino acid sequence PLARTLSVAGLPGKK (**SEQ ID NO. 11**) was utilized. The production of ADP from ATP that accompanies phosphoryl transfer to the substrate was coupled to oxidation of NADH using phosphoenolpyruvate (PEP) through the actions of pyruvate kinase (PK) and lactic dehydrogenase (LDH). The oxidation of NADH was monitored by following the decrease of absorbance at 340 nm (e340=6.22 cm-1 mM-1) using a HP8452 spectrophotometer. Typical reaction solutions contained: 4 mM PEP, 0.15 mM NADH, 28 units of LDH/mL, 16 units of PK/mL, 3 mM DTT, 0. 125 mM Syntide-2, 0.15 mM ATP and 25 mM $MgCl_2$ in 50 mM TRIS pH 7.5; 400 mM NaCl. Assays were initiated with 10 nM of kinase domain of Chk1, KH289. K_i values were determined by measuring initial enzyme activity in the presence of varying concentrations of inhibitors. The data were analyzed using Enzyme Kinetic and Kaleidagraph software.

[0168] The table below (**Table 3**) compares three different preparations of Chk1. The first preparation is the full length form, which comprises amino acids 1-476 of **SEQ ID NO. 2.** The next preparation contains proteolytically cleaved fragments, a mixture of Chk1 protein fragments obtained from the full-length protein during fermentation. The exact enzymes involved and cleavage site generated for these fragments is unknown. However, analysis of the fragments indicated that one of them is similar in size to the 1-289. The third preparation is the kinase domain of amino acids 1-289 of **SEQ ID NO. 2** (KH289) As mentioned above, the assay used detects the ADP product by coupling through the enzymatic actions of pyruvate kinase and lactate dehydrogenase.

Table 3

Prep No.	Prep	Concentration	Rate/min	Activity	Ki
HA2-013	Full Length Chk1	75nM	0.0190	1 (control)	48 ± 1nM
HA2-022	Proteolytically cleaved Chk1	2nM	0.0208	+38 fold	37 ± 5 nM
HB2-061	Kinase Domain Chk1 (1-289)	7.3nM	0.0200	+10 fold	68 ± 12 nM

[0169] Additional activity comparison experiments were performed using new preparations of full length Chk1, proteolitically cleaved Chk1, and kinase domain Chk1. The preparation conditions were as described above. Once again, the cleaved preparation was 38 fold more active than the non-cleaved preparation.

10. High Throughput Screens

[0170] The following substrates were tested for peptide content and activity:•

Table 4

Peptide Substrates			
		Activity	Peptide
Syntide 2	PLARTLSVAGLPGKK (SEQ ID NO. 11)	100%	75%
Syntide 3	KAGAG-PLARTLSVAGLPG-Biotin-K (SEQ ID NO. 12)	67%	50%
Syntide 4	Ac - PLARTLSVAGLPG-AGAGAGAK (SEQ ID NO. 13)	72%	45%
Syntide 5	PLARTLS (PO_3) VAGLPGKK (SEQ ID NO. 15)	NT	42%
Syntide 6	PLARTLS (PO_3) VGALPGK (Biotin) (SEQ ID NO. 16)	NT	77%

[0171] As described in detail below, an aspect of the invention involves a nonradioactive ELISA based assay suitable for high throughput screening (HTS). The development of the ELISA based CHK1 kinase HTS assay was first initiated with a monoclonal anti-phosphoserine antibody called Clone PSR-45, supplied by Sigma. New Chk peptide

substrates, analogues of Syntide2, were synthesized to validate this assay. These peptides are listed in Table 4. Biotin-Syntide-2 (**SEQ ID NO. 12**), and N-terminus acetylated Syntide-2 (**SEQ ID NO. 13**) and the expected peptide products after CHK phosphorylation, serine phosphorylated Syntide 2 (**SEQ ID NO. 15**), and serine phospholylated biotin-Syntide 2 (**SEQ ID NO. 16**) were synthesized for assay development. Although the assay worked well in solution with these peptides, it did not work when the peptide (serine phosphorylated Syntide 2 — **SEQ ID NO. 15**) was immobilized on DNA BIND (Costar) 96 well plates. This antibody also did not work well when the biotin-labeled peptide was immobilized using Neutravidin coated 96 well plates (Pierce). To circumvent these issues, a polyclonal antibody specifically directed against phosphorylated Syntide-2 (**SEQ ID NO. 15**) was raised in rabbits. The rabbit polyclonal antiphosphosyntide antibody was found to quantitatively and specifically recognize phosphoserine on both Syntide 2-Ser-PO_3 (assay on DNA BIND plates) or on biotin-Syntide 2-Ser-PO_3 (assayed on Neutravidin coated 96 well plates) when compared with the unphosphorylated peptide counterparts. A modified Chk1 HTS assay ELISA was developed using His-tagged KH289 Chk1 kinase, biotinsyntide substrate assayed on Neutravidin coated 96 well plates, and the rabbit anti-phosphosyntide antibody to detect the phosphorylated product.

[0172] This Chk1 kinase ELISA HTS allowed for the robotic screening of compound libraries. Herein, the Beckman robotics station was used. First; the Chk1 kinase was assayed in Neutravidin coated 96-well plates in 100 µL/well of reaction mixture. The reaction mixture comprised 50 mM Tris-HCl (pH 7.5), 10 mM $MgCl_2$, 3 mM DTT, 400 mM NaCl, 50 µM ATP, 10 µM biotin-Syntide 2 peptide substrate and 10 nM Chk1 kinase (KH289). The assay was performed both with and without 20 µM test compound. Herein, the biotin Syntide 2 substrate had the following sequence: PLARTLSVAGLPGK-biotin-K (**SEQ ID NO. 12**).

[0173] The assay is depicted in **Figure 10**. In step A, 93 µL of reaction mixture (less both the Chk1 kinase and the biotin-syntide) is added, followed by the addition of 2 µL of test compound (20 µM final). The kinase reaction is initiated by the addition of 5 µL of enzyme-substrate stock (200 nM Chk1 kinase and 200 µM biotin-syntide). The kinase reaction is allowed to proceed for 10 min at room temperature (≅ 22 °C) as shown in Step B. Following 10 minutes of kinase reaction, both phosphorylated and unphosphorylated biotin-Syntide 2 are bound to the Neutravidin coated plate. In step C, the plates are washed with PBS/Tween-20 to terminate the kinase reaction and to remove the unbound phosphorylated or non-phosphorylated biotin- Syntide 2. In step D, the plates are incubated at room temperature for 60 minutes with rabbit anti-phosphosyntide antibody (1: 40,000 dilution; 100 µL/well). The anti-phosphosyntide antibody binds specifically to the serine-phosphorylated biotin-Syntide 2. The unbound antibody is removed with washes of PBS/Tween-20. The plates are then incubated at room temperature for 60 minutes with goat-anti-rabbit-IgG(Fc)-HRP (horseradish peroxidase) antibody. In step E, the plates are washed with PBS/Tween to remove the unbound secondary antibody. Then, 100 µL/well chromogenic dye ABTS (HRP substrate) is added. The color development, resulting from the HRP reaction, is allowed to take place for 18 minutes. This is followed by absorbance measurement at 405 nm in a 96-well plate reader. The Chk1 kinase activity is directly proportional to the optical density of the color formed.

[0174] All references cited herein are incorporated by reference in their entirety.

[0175] While the invention has been described in conjunction with examples thereof it is to be understood that the foregoing description is exemplary and explanatory in nature, and is intended to illustrate the invention and its preferred embodiments. Through routine experimentation, the artisan will recognize apparent modifications and variations that may be made without departing from the spirit of the invention. Thus, the invention is intended to be defined not by the above description, but by the following claims and their equivalents.

SEQUENCE LISTINGS

[0176]

SEQ ID NO. 1 — full length human Chk1 (nucleotide sequence — 1933 base pairs)
SEQ ID NO. 2 — full length human Chk1 (peptide sequence - 476 AA)
SEQ ID NO. 3 — PCR primer (chk6w)
SEQ ID NO. 4 — PCR primer (KH289)
SEQ ID NO. 5 — PCR primer (K289)
SEQ ID NO. 6 — PCR primer (Chk11)
SEQ ID NO. 7 — PCR primer (K210)
SEQ ID NO. 8 — PCR primer (KH210)
SEQ ID NO. 9 — PCR primer (K248)
SEQ ID NO. 10 — PCR primer (KH248)
SEQ ID NO. 11 — synthetic substrate peptide, Syntide-2
SEQ ID NO. 12 — synthetic substrate peptide, Syntide-3
SEQ ID NO. 13 — synthetic substrate peptide, Syntide-4
SEQ ID NO. 14 — oligonucleotide primer

SEQ ID NO. 15 — serine phosphorylated Syntide-2

SEQ ID NO. 16 — serine phosphoxylated biotin Syntide-2

SEQ ID NO. 17 —peptide sequence for Cdc25 protein phosphatase

SEQ ID NO. 18 —peptide sequence for mouse (mm) Chk1 kinase domain

SEQ ID NO. 19 —peptide sequence for Xenopus (x1) Chk1 kinase domain

SEQ ID NO. 20 —peptide sequence for fruit fly (dm) Chk1 kinase domain

SEQ ID NO. 21 —peptide sequence for C. elegans (ce) Chk1 kinase domain

SEQ ID NO. 22 —peptide sequence for S. cerevisiae (sc) Chk1 kinase domain

SEQ ID NO. 23 —peptide sequence for S. pombe (sp) Chk1 kinase domain

SEQ ID NO. 24 —conserved motif AQXFFXQL for Chk1 kinase domain, helix _E (residues 107-114)

SEQUENCE LISTING

<110> Agouron Pharmaceuticals, Inc.

<120> Catalytic Domain of the Human Effector Cell cycle Checkpoint Protein Kinase, Chk1, Materials and Methods for Identification of Inhibitors Thereof

<130> 30189

<150> 60/162,887
<151> 1999-11-01

<150> 09/460,421
<151> 1999-12-14

<160> 24

<170> PatentIn Ver. 2.1

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<213> Homo sapiens

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ttatcaatgc ctgaaagaga cttgtgagaa gttgggctat caatggaaga aaagttgtat 1260
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agtgctgcta tgttgacatt attcttccta gagaagatta tcctgtcctg caaactgcaa 1560
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ttgttcggca tacaaataat acctatatct taattgtaag caaaactttg gggaaaggat 1680
gaatagaatt catttgatta tttcttcatg tgtgtttagt atctgaattt gaaactcatc 1740
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<210> 2
<211> 476
<212> PRT
<213> Homo sapiens

<400> 2

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Met Ala Val Pro Phe Val Glu Asp Trp Asp Leu Val Gly Thr Leu Gly
 1               5                  10                  15

Glu Gly Ala Tyr Gly Glu Val Gln Leu Ala Val Asn Arg Val Thr Glu
            20                  25                  30

Glu Ala Val Ala Val Lys Ile Val Asp Met Lys Arg Ala Val Asp Cys
        35                  40                  45

Pro Glu Asn Ile Lys Lys Glu Ile Cys Ile Asn Lys Met Leu Asn His
    50                  55                  60

Glu Asn Val Val Lys Phe Tyr Gly His Arg Arg Glu Gly Asn Ile Gln
65                  70                  75                  80

Tyr Leu Phe Leu Glu Tyr Cys Ser Gly Gly Glu Leu Phe Asp Arg Ile
                85                  90                  95

Glu Pro Asp Ile Gly Met Pro Glu Pro Asp Ala Gln Arg Phe Phe His
            100                 105                 110

Gln Leu Met Ala Gly Val Val Tyr Leu His Gly Ile Gly Ile Thr His
        115                 120                 125

Arg Asp Ile Lys Pro Glu Asn Leu Leu Leu Asp Glu Arg Asp Asn Leu
    130                 135                 140

Lys Ile Ser Asp Phe Gly Leu Ala Thr Val Phe Arg Tyr Asn Asn Arg
145                 150                 155                 160

Glu Arg Leu Leu Asn Lys Met Cys Gly Thr Leu Pro Tyr Val Ala Pro
                165                 170                 175

Glu Leu Leu Lys Arg Arg Glu Phe His Ala Glu Pro Val Asp Val Trp
            180                 185                 190

Ser Cys Gly Ile Val Leu Thr Ala Met Leu Ala Gly Glu Leu Pro Trp
        195                 200                 205

Asp Gln Pro Ser Asp Ser Cys Gln Glu Tyr Ser Asp Trp Lys Glu Lys
    210                 215                 220

Lys Thr Tyr Leu Asn Pro Trp Lys Lys Ile Asp Ser Ala Pro Leu Ala
225                 230                 235                 240

Leu Leu His Lys Ile Leu Val Glu Asn Pro Ser Ala Arg Ile Thr Ile
                245                 250                 255

Pro Asp Ile Lys Lys Asp Arg Trp Tyr Asn Lys Pro Leu Lys Lys Gly
            260                 265                 270

Ala Lys Arg Pro Arg Val Thr Ser Gly Gly Val Ser Glu Ser Pro Ser
        275                 280                 285

Gly Phe Ser Lys His Ile Gln Ser Asn Leu Asp Phe Ser Pro Val Asn
    290                 295                 300

Ser Ala Ser Ser Glu Glu Asn Val Lys Tyr Ser Ser Ser Gln Pro Glu
305                 310                 315                 320

Pro Arg Thr Gly Leu Ser Leu Trp Asp Thr Ser Pro Ser Tyr Ile Asp
```

325 330 335

Lys Leu Val Gln Gly Ile Ser Phe Ser Gln Pro Thr Cys Pro Asp His
340 345 350

Met Leu Leu Asn Ser Gly Leu Leu Gly Thr Pro Gly Ser Ser Gln Asn
355 360 365

Pro Trp Gln Arg Leu Val Lys Arg Met Thr Arg Phe Phe Thr Lys Leu
370 375 380

Asp Ala Asp Lys Ser Tyr Gln Cys Leu Lys Glu Thr Cys Glu Lys Leu
385 390 395 400

Gln Tyr Gln Trp Lys Lys Ser Cys Met Asn Gln Val Thr Ile Ser Thr
405 410 415

Thr Asp Arg Arg Asn Asn Lys Leu Ile Phe Lys Val Asn Leu Leu Glu
420 425 430

Met Asp Asp Lys Ile Leu Val Asp Phe Arg Leu Ser Lys Gly Asp Gly
435 440 445

Leu Glu Phe Lys Arg His Phe Leu Lys Ile Lys Gly Lys Leu Ile Asp
450 455 460

Ile Val Ser Ser Gln Lys Val Trp Leu Pro Ala Thr
465 470 475

<210> 3
<211> 34
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer

<400> 3
gagctcagta ccatctatct tttttgatgt ctgg 34

<210> 4
<211> 47
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer

<400> 4
gagctcagtt ggtggtggtg gtggtgtcca ctgggagact ctgacac 47

<210> 5
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer

<400> 5

gagctcatcc actgggagac tctgacac 28

<210> 6
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer

<400> 6
ccatggagct caagaaaggg gcaaaaagg 29

<210> 7
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer

<400> 7
gagctcattg gtcccatggc aattctcc 28

<210> 8
<211> 46
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer

<400> 8
gagctcagtg gtggtggtgg tggtggtggt cccatggcaa ttctcc 46

<210> 9
<211> 31
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer

<400> 9
gagctcactc aactaagatt ttatgcagca g 31

<210> 10
<211> 49
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer

<400> 10
gagctcagtg gtggtggtgg tggtgctcaa ctaagatttt atgcagcag 49

<210> 11
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<400> 11
Pro Leu Ala Arg Thr Leu Ser Val Ala Gly Leu Pro Gly Lys Lys
1 5 10 15

<210> 12
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<220>
<223> Biotinylated

<400> 12
Lys Ala Gly Ala Gly Pro Leu Ala Arg Thr Leu Ser Val Ala Gly Leu
1 5 10 15

Pro Gly Lys

<210> 13
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<400> 13
Pro Leu Ala Arg Thr Leu Ser Val Ala Gly Leu Pro Gly Ala Gly Ala
1 5 10 15

Gly Ala Gly Ala Lys
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<210> 14
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: oligonucleotide primer

<400> 14
tgaataatcc ggcatatgta taggtttttt 30

<210> 15
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<220>
<221> MOD_RES
<222> (7)
<223> phosphorylated serine

<400> 15
Pro Leu Ala Arg Thr Leu Ser Val Ala Gly Leu Pro Gly Lys Lys
1 5 10 15

<210> 16
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: synthetic peptide

<220>
<221> MOD_RES
<222> (7)
<223> phosphorylated serine

<220>
<223> Biotinylated

<400> 16
Pro Leu Ala Arg Thr Leu Ser Val Gly Ala Leu Pro Gly Lys
1 5 10

<210> 17
<211> 473
<212> PRT
<213> Homo sapiens

<400> 17
Met Ser Thr Glu Leu Phe Ser Ser Thr Arg Glu Glu Gly Ser Ser Gly
1 5 10 15

Ser Gly Pro Ser Phe Arg Ser Asn Gln Arg Lys Met Leu Asn Leu Leu
20 25 30

Leu Glu Arg Asp Thr Ser Phe Thr Val Cys Pro Asp Val Pro Arg Thr
35 40 45

Pro Val Gly Lys Phe Leu Gly Asp Ser Ala Asn Leu Ser Ile Leu Ser
50 55 60

Gly Gly Thr Pro Lys Cys Cys Leu Asp Leu Ser Asn Leu Ser Ser Gly
65 70 75 80

```
Glu Ile Thr Ala Thr Gln Leu Thr Thr Ser Ala Asp Leu Asp Glu Thr
                  85                  90                  95

Gly His Leu Asp Ser Ser Gly Leu Gln Glu Val His Leu Ala Gly Met
             100                 105                 110

Asn His Asp Gln His Leu Met Lys Cys Ser Pro Ala Gln Leu Leu Cys
         115                 120                 125

Ser Thr Pro Asn Gly Leu Asp Arg Gly His Arg Lys Arg Asp Ala Met
     130                 135                 140

Cys Ser Ser Ser Ala Asn Lys Glu Asn Asp Asn Gly Asn Leu Val Asp
145                 150                 155                 160

Ser Glu Met Lys Tyr Leu Gly Ser Pro Ile Thr Thr Val Pro Lys Leu
                165                 170                 175

Asp Lys Asn Pro Asn Leu Gly Glu Asp Gln Ala Glu Glu Ile Ser Asp
            180                 185                 190

Glu Leu Met Glu Phe Ser Leu Lys Asp Gln Glu Ala Lys Val Ser Arg
        195                 200                 205

Ser Gly Leu Tyr Arg Ser Pro Ser Met Pro Glu Asn Leu Asn Arg Pro
    210                 215                 220

Arg Leu Lys Gln Val Glu Lys Phe Lys Asp Asn Thr Ile Pro Asp Lys
225                 230                 235                 240

Val Lys Lys Lys Tyr Phe Ser Gly Gln Gly Lys Leu Arg Lys Gly Leu
                245                 250                 255

Cys Leu Lys Lys Thr Val Ser Leu Cys Asp Ile Thr Ile Thr Gln Met
            260                 265                 270

Leu Glu Glu Asp Ser Asn Gln Gly His Leu Ile Gly Asp Phe Ser Lys
        275                 280                 285

Val Cys Ala Leu Pro Thr Val Ser Gly Lys His Gln Asp Leu Lys Tyr
    290                 295                 300

Val Asn Pro Glu Thr Val Ala Ala Leu Leu Ser Gly Lys Phe Gln Gly
305                 310                 315                 320

Leu Ile Glu Lys Phe Tyr Val Ile Asp Cys Arg Tyr Pro Tyr Glu Tyr
                325                 330                 335

Leu Gly Gly His Ile Gln Gly Ala Leu Asn Leu Tyr Ser Gln Glu Glu
            340                 345                 350

Leu Phe Asn Phe Phe Leu Lys Lys Pro Ile Val Pro Leu Asp Thr Gln
        355                 360                 365

Lys Arg Ile Ile Ile Val Phe His Cys Glu Phe Ser Ser Glu Arg Gly
    370                 375                 380

Pro Arg Met Cys Arg Cys Leu Arg Glu Glu Asp Arg Ser Leu Asn Gln
385                 390                 395                 400

Tyr Pro Ala Leu Tyr Tyr Pro Glu Leu Tyr Ile Leu Lys Gly Gly Tyr
                405                 410                 415
```

```
Arg Asp Phe Phe Pro Glu Tyr Met Glu Leu Cys Glu Pro Gln Ser Tyr
            420                 425                 430

Cys Pro Met His His Gln Asp His Lys Thr Glu Leu Leu Arg Cys Arg
        435                 440                 445

Ser Gln Ser Lys Val Gln Glu Gly Glu Arg Gln Leu Arg Glu Gln Ile
    450                 455                 460

Ala Leu Leu Val Lys Asp Met Ser Pro
465                 470
```

<210> 18
<211> 289
<212> PRT
<213> Murine sp.

<400> 18

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Met Ala Val Pro Phe Val Glu Asp Trp Asp Leu Val Gln Thr Leu Gly
  1               5                  10                  15

Glu Gly Ala Tyr Gly Glu Val Gln Leu Ala Val Asn Arg Ile Thr Glu
             20                  25                  30

Gln Ala Val Ala Val Lys Ile Val Asp Met Lys Arg Ala Ile Asp Cys
         35                  40                  45

Pro Gln Asn Ile Lys Lys Glu Ile Cys Ile Asn Lys Met Leu Ser His
     50                  55                  60

Glu Asn Val Val Lys Phe Tyr Gly His Arg Arg Glu Gly His Ile Gln
 65                  70                  75                  80

Tyr Leu Phe Leu Glu Tyr Cys Ser Gly Gly Glu Leu Phe Asp Arg Ile
                 85                  90                  95

Glu Pro Asp Ile Gly Met Pro Glu Gln Asp Ala Gln Arg Phe Phe His
            100                 105                 110

Gln Leu Met Ala Gly Val Val Tyr Leu His Gly Ile Gly Ile Thr His
        115                 120                 125

Arg Asp Ile Lys Pro Glu Asn Leu Leu Leu Asp Glu Arg Asp Asn Leu
    130                 135                 140

Lys Ile Ser Asp Phe Gly Leu Ala Thr Val Phe Arg His Asn Asn Arg
145                 150                 155                 160

Glu Arg Leu Leu Asn Lys Met Cys Gly Thr Leu Pro Tyr Val Ala Pro
                165                 170                 175

Glu Leu Leu Lys Arg Lys Glu Phe His Ala Glu Pro Val Asp Val Trp
            180                 185                 190

Ser Cys Gly Ile Val Leu Thr Ala Met Leu Ala Gly Glu Leu Pro Trp
        195                 200                 205

Asp Gln Pro Ser Asp Ser Cys Gln Glu Tyr Ser Asp Trp Lys Glu Lys
    210                 215                 220

Lys Thr Tyr Leu Asn Pro Trp Lys Lys Ile Asp Ser Ala Pro Leu Ala
225                 230                 235                 240
```

```
Leu Leu His Lys Ile Leu Val Glu Thr Pro Ser Ala Arg Ile Thr Ile
                245                 250                 255

Pro Asp Ile Lys Lys Asp Arg Trp Tyr Asn Lys Pro Leu Asn Arg Gly
            260                 265                 270

Ala Lys Arg Pro Arg Ala Thr Ser Gly Gly Met Ser Glu Ser Ser Ser
        275                 280                 285

Gly
```

<210> 19
<211> 286
<212> PRT
<213> Xenopus sp.

<400> 19

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Met Ala Val Pro Phe Val Glu Asp Trp Asp Leu Val Gln Thr Leu Gly
  1               5                  10                  15

Glu Gly Ala Tyr Gly Glu Val Gln Leu Ala Val Asn Arg Lys Thr Glu
             20                  25                  30

Glu Ala Val Ala Val Lys Ile Val Asp Met Thr Arg Ala Ala Asp Cys
         35                  40                  45

Pro Glu Asn Ile Lys Lys Glu Ile Cys Ile Asn Arg Met Leu Ser His
     50                  55                  60

Thr Asn Ile Val Arg Phe Tyr Gly His Arg Arg Glu Gly Asn Ile Gln
 65                  70                  75                  80

Tyr Leu Phe Leu Glu Tyr Cys Arg Gly Gly Glu Leu Phe Asp Arg Ile
                85                  90                  95

Glu Pro Asp Val Gly Met Pro Glu Gln Asp Ala Gln Lys Phe Phe Gln
            100                 105                 110

Gln Leu Ile Ala Gly Val Glu Tyr Leu His Ser Ile Gly Ile Thr His
        115                 120                 125

Arg Asp Ile Lys Pro Glu Asn Leu Leu Leu Asp Glu Arg Asp Gln Leu
    130                 135                 140

Lys Ile Ser Asp Phe Gly Leu Ala Thr Val Phe Arg His Asn Gly Lys
145                 150                 155                 160

Glu Arg Leu Leu Ser Lys Met Cys Gly Thr Leu Pro Tyr Val Ala Pro
                165                 170                 175

Glu Leu Ile Lys Ser Arg Ala Phe His Ala Asp Pro Val Asp Val Trp
            180                 185                 190

Ser Cys Gly Ile Val Leu Thr Ala Met Leu Ala Gly Glu Leu Pro Trp
        195                 200                 205

Asp Gln Pro Asn Glu Val Cys Gln Glu Tyr Cys Asp Trp Lys Glu Lys
    210                 215                 220

Asn His Tyr Leu Thr Pro Trp Lys Lys Ile Ser Ala Thr Pro Leu Ala
```

225 230 235 240

Leu Leu Gly Lys Met Leu Thr Glu Asn Pro Gln Ser Arg Ile Thr Ile
245 250 255

Pro Asp Ile Lys Lys Asp Arg Trp Phe Thr Glu Ile Ile Lys Lys Gly
260 265 270

Leu Lys Arg Ser Arg Val Ile Ser Gly Gly Ser Ser Asp Ser Ser Val
275 280 285

<210> 20
<211> 305
<212> PRT
<213> Drosophila sp.

<400> 20
Met Ala Ala Thr Leu Thr Glu Ala Gly Thr Gly Pro Ala Ala Thr Arg
1 5 10 15

Glu Phe Val Glu Gly Trp Thr Leu Ala Gln Thr Leu Gly Glu Gly Ala
20 25 30

Tyr Gly Glu Val Lys Leu Leu Ile Asn Arg Gln Thr Gly Gly Gly Cys
35 40 45

Gly Met Lys Met Val Asp Leu Lys Lys His Pro Asp Ala Ala Asn Ser
50 55 60

Val Arg Lys Glu Val Cys Ile Gln Lys Met Leu Gln Asp Lys His Ile
65 70 75 80

Leu Arg Phe Phe Gly Lys Arg Ser Gln Gly Ser Val Glu Tyr Ile Phe
85 90 95

Leu Glu Tyr Ala Ala Gly Gly Glu Leu Phe Asp Arg Ile Glu Pro Asp
100 105 110

Val Gly Met Pro Gln His Glu Ala Gln Arg Tyr Phe Thr Gln Leu Leu
115 120 125

Ser Gly Leu Asn Tyr Leu His Gln Arg Gly Ile Ala His Arg Asp Leu
130 135 140

Lys Pro Glu Asn Leu Leu Leu Asp Glu His Asp Asn Val Lys Ile Ser
145 150 155 160

Asp Phe Gly Met Ala Thr Met Phe Arg Cys Lys Gly Lys Glu Arg Leu
165 170 175

Leu Asp Lys Arg Cys Gly Thr Leu Pro Tyr Val Ala Pro Glu Val Leu
180 185 190

Gln Lys Ala Tyr Gln Pro Gln Pro Ala Asp Leu Trp Ser Cys Gly Val
195 200 205

Ile Leu Val Thr Met Leu Ala Gly Glu Leu Pro Trp Asp Gln Pro Ser
210 215 220

Thr Asn Cys Thr Glu Phe Thr Asn Trp Arg Asp Asn Asp His Trp Gln
225 230 235 240

```
Leu Gln Thr Pro Trp Ser Lys Leu Asp Thr Leu Ala Ile Ser Leu Leu
                245                 250                 255

Arg Lys Leu Leu Leu Ala Thr Ser Pro Gly Thr Arg Leu Thr Leu Glu
            260                 265                 270

Lys Thr Leu Asp His Lys Trp Cys Asn Met Gln Phe Ala Asp Asn Glu
        275                 280                 285

Arg Ser Tyr Asp Leu Val Asp Ser Ala Ala Ala Leu Glu Ile Cys Ser
    290                 295                 300

Pro
305
```

<210> 21
<211> 299
<212> PRT
<213> C. elegans

<400> 21

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Met Ser Ala Ala Ser Thr Thr Ser Thr Pro Ala Ala Ala Ala Val Ala
  1               5                  10                  15

Pro Gln Gln Pro Glu Ser Leu Tyr Arg Val Val Gln Thr Leu Gly Glu
            20                  25                  30

Gly Ala Phe Gly Glu Val Leu Leu Ile Val Asn Thr Lys Asn Pro Glu
        35                  40                  45

Val Ala Ala Ala Met Lys Lys Ile Asn Ile Ala Asn Lys Ser Lys Asp
    50                  55                  60

Phe Ile Asp Asn Ile Arg Lys Glu Tyr Leu Leu Gln Lys Arg Val Ser
65                  70                  75                  80

Ala Val Gly His Asp Asn Val Ile Arg Met Ile Gly Met Arg Asn Asp
                85                  90                  95

Pro Gln Phe Tyr Tyr Leu Phe Leu Glu Tyr Ala Asp Gly Gly Glu Leu
            100                 105                 110

Phe Asp Lys Ile Glu Pro Asp Cys Gly Met Ser Pro Val Phe Ala Gln
        115                 120                 125

Phe Tyr Phe Lys Gln Leu Ile Cys Gly Leu Lys Phe Ile His Asp Asn
    130                 135                 140

Asp Val Val His Arg Asp Ile Lys Pro Glu Asn Leu Leu Leu Thr Gly
145                 150                 155                 160

Thr His Val Leu Lys Ile Ser Asp Phe Gly Met Ala Thr Leu Tyr Arg
                165                 170                 175

Asn Lys Gly Glu Glu Arg Leu Leu Asp Leu Ser Cys Gly Thr Ile Pro
            180                 185                 190

Tyr Ala Ala Pro Glu Leu Cys Ala Gly Lys Lys Tyr Arg Gly Pro Pro
        195                 200                 205

Val Asp Val Trp Ser Ser Gly Ile Val Leu Ile Ala Met Leu Thr Gly
    210                 215                 220
```

```
Glu Leu Pro Trp Asp Arg Ala Ser Asp Ala Ser Gln Ser Tyr Met Gly
225                 230                 235                 240

Trp Ile Ser Asn Thr Ser Leu Asp Glu Arg Pro Trp Lys Lys Ile Asp
                245                 250                 255

Val Arg Ala Leu Cys Met Leu Arg Lys Ile Val Thr Asp Lys Thr Asp
            260                 265                 270

Lys Arg Ala Thr Ile Glu Gln Ile Gln Ala Asp Pro Trp Tyr Gln His
        275                 280                 285

Asn Phe Gly Gln Val Glu Thr Pro Asn Gly Arg
    290                 295
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<210> 22
<211> 306
<212> PRT
<213> S. cerevisiae

<400> 22

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Met Ser Leu Ser Gln Val Ser Pro Leu Pro His Ile Lys Asp Val Val
  1               5                  10                  15

Leu Gly Asp Thr Val Gly Gln Gly Ala Phe Ala Cys Val Lys Asn Ala
            20                  25                  30

His Leu Gln Met Asp Pro Ser Ile Ile Leu Ala Val Lys Phe Ile His
        35                  40                  45

Val Pro Thr Cys Lys Lys Met Gly Leu Ser Asp Lys Asp Ile Thr Lys
    50                  55                  60

Glu Val Val Leu Gln Ser Lys Cys Ser Lys His Pro Asn Val Leu Arg
65                  70                  75                  80

Leu Ile Asp Cys Asn Val Ser Lys Glu Tyr Met Trp Ile Ile Leu Glu
                85                  90                  95

Met Ala Asp Gly Gly Asp Leu Phe Asp Lys Ile Glu Pro Asp Val Gly
            100                 105                 110

Val Asp Ser Asp Val Ala Gln Phe Tyr Phe Gln Gln Leu Val Ser Ala
        115                 120                 125

Ile Asn Tyr Leu His Val Glu Cys Gly Val Ala His Arg Asp Ile Lys
    130                 135                 140

Pro Glu Asn Ile Leu Leu Asp Lys Asn Gly Asn Leu Lys Leu Ala Asp
145                 150                 155                 160

Phe Gly Leu Ala Ser Gln Phe Arg Arg Lys Asp Gly Thr Leu Arg Val
                165                 170                 175

Ser Met Asp Gln Arg Gly Ser Pro Pro Tyr Met Ala Pro Glu Val Leu
            180                 185                 190

Tyr Ser Glu Glu Gly Tyr Tyr Ala Asp Arg Thr Asp Ile Trp Ser Ile
        195                 200                 205

Gly Ile Leu Leu Phe Val Leu Leu Thr Gly Gln Thr Pro Trp Glu Leu
```

```
    210                 215                 220

Pro Ser Leu Glu Asn Glu Asp Phe Val Phe Phe Ile Glu Asn Asp Gly
225                 230                 235                 240

Asn Leu Asn Trp Gly Pro Trp Ser Lys Ile Glu Phe Thr His Leu Asn
                245                 250                 255

Leu Leu Arg Lys Ile Leu Gln Pro Asp Pro Asn Lys Arg Val Thr Leu
            260                 265                 270

Lys Ala Leu Lys Leu His Pro Trp Val Leu Arg Arg Ala Ser Phe Ser
        275                 280                 285

Gly Asp Asp Gly Leu Cys Asn Asp Pro Glu Leu Leu Ala Lys Lys Leu
    290                 295                 300

Phe Ser
305
```

<210> 23
<211> 295
<212> PRT
<213> S. pombe

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<400> 23
Met Ala Gln Lys Leu Asp Asn Phe Pro Tyr His Ile Gly Arg Glu Ile
  1               5                  10                  15

Gly Thr Gly Ala Phe Ala Ser Val Arg Leu Cys Tyr Asp Asp Asn Ala
            20                  25                  30

Lys Ile Tyr Ala Val Lys Phe Val Asn Lys Lys His Ala Thr Ser Cys
        35                  40                  45

Met Asn Ala Gly Val Trp Ala Arg Arg Met Ala Ser Glu Ile Gln Leu
    50                  55                  60

His Lys Leu Cys Asn Gly His Lys Asn Ile Ile His Phe Tyr Asn Thr
65                  70                  75                  80

Ala Glu Asn Pro Gln Trp Arg Trp Val Val Leu Glu Phe Ala Gln Gly
                85                  90                  95

Gly Asp Leu Phe Asp Lys Ile Glu Pro Asp Val Gly Ile Asp Glu Asp
            100                 105                 110

Val Ala Gln Phe Tyr Phe Ala Gln Leu Met Glu Gly Ile Ser Phe Met
        115                 120                 125

His Ser Lys Gly Val Ala His Arg Asp Leu Lys Pro Glu Asn Ile Leu
    130                 135                 140

Leu Asp Tyr Asn Gly Asn Leu Lys Ile Ser Asp Phe Gly Phe Ala Ser
145                 150                 155                 160

Leu Phe Ser Tyr Lys Gly Lys Ser Arg Leu Leu Asn Ser Pro Val Gly
                165                 170                 175

Ser Pro Pro Tyr Ala Ala Pro Glu Ile Thr Gln Gln Tyr Asp Gly Ser
            180                 185                 190
```

```
Lys Val Asp Val Trp Ser Cys Gly Ile Ile Leu Phe Ala Leu Leu Leu
        195                 200                 205

Gly Asn Thr Pro Trp Asp Glu Ala Ile Ser Asn Thr Gly Asp Tyr Leu
    210                 215                 220

Leu Tyr Lys Lys Gln Cys Glu Arg Pro Ser Tyr His Pro Trp Asn Leu
225                 230                 235                 240

Leu Ser Pro Gly Ala Tyr Ser Ile Ile Thr Gly Met Leu Arg Ser Asp
                245                 250                 255

Pro Phe Lys Arg Tyr Ser Val Lys His Val Val Gln His Pro Trp Leu
            260                 265                 270

Thr Ser Ser Thr Pro Phe Arg Thr Lys Asn Gly Asn Cys Ala Asp Pro
        275                 280                 285

Val Ala Leu Ala Ser Arg Leu
    290                 295


<210> 24
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: conserved
      motif

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<220>
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<400> 24
Ala Gln Xaa Phe Phe Xaa Gln Leu
  1               5
```

Claims

1. A composition comprising an isolated, purified polynucleotide which encodes the active form of the human Chk1 kinase or a functional, active human Chk1 kinase analog thereof.

2. The composition according to claim 1, wherein the nucleotide sequence of said polynucleotide comprises bases 35 to 830 of SEQ ID NO. 1 or a functional, active mutant or variant thereof.

3. A polypeptide in a crystallized form comprising the catalytically active form of the human Chk1 kinase and the inhibitor binding site thereof.

4. The polypeptide according to claim 3 wherein the crystal is solved to a resolution of at least 2.5 Å.

5. The polypeptide according to claim 3 wherein the crystal is solved to a resolution of at least 2.0 Å.

6. The polypeptide according to claim 3 wherein the crystal is solved to a resolution of about 1.7 Å.

7. The polypeptide according to claim 3 wherein the amino acid sequence of said polypeptide comprises amino acids 16 to 265 of SEQ ID NO. 2 or an active mutant or variant thereof.

8. The polypeptide according to claim 3 wherein the amino acid sequence of said polypeptide comprises amino acids 16 to 289 of SEQ ID NO. 2 or an active mutant or variant thereof.

9. The polypeptide according to claim 3 wherein the amino acid sequence of said polypeptide comprises amino acids 16 to 291 of SEQ ID NO. 2 or an active mutant or variant thereof.

10. The polypeptide according to claim 3 wherein the amino acid sequence of said polypeptide comprises amino acids 1 to 265 of SEQ ID NO. 2 or an active mutant or variant thereof.

11. The polypeptide according to claim 3 wherein the amino acid sequence of said polypeptide comprises amino acids 1 to 289 of SEQ ID NO. 2 or an active mutant or variant thereof.

12. The polypeptide according to claim 3 wherein the amino acid sequence of said polypeptide comprises amino acids 1 to 291 of SEQ ID NO. 2 or an active mutant or variant thereof.

13. The polypeptide according to claim 3 wherein said polypeptide further comprises a six histidine tag on the C-terminal thereof.

14. An isolated, soluble, catalytically active polypeptide comprising the active form of the human Chk1 kinase or a functional, active human Chk1 kinase analog thereof.

15. The polypeptide according to claim 14 comprising the full length human Chk1 protein having the C-terminal portion thereof deleted so as yield the human Chk1 kinase domain in its active configuration.

16. The polypeptide according to claim 14 wherein said polypeptide comprises amino acids 16 to 265 of the sequence as set forth in SEQ ID NO. 2 or a conservatively substituted variant thereof.

17. The polypeptide according to claim 14 wherein said polypeptide comprises amino acids 16 to 289 of the sequence as set forth in SEQ ID NO. 2 or a conservatively substituted variant thereof.

18. The polypeptide according to claim 14 wherein said polypeptide comprises amino acids 16 to 291 of the sequence as set forth in SEQ ID NO. 2 or a conservatively substituted variant thereof.

19. The polypeptide according to claim 14 wherein said polypeptide comprises amino acids 1 to 265 of the sequence as set forth in SEQ ID NO.2 or a conservatively substituted variant thereof.

20. The polypeptide according to claim 14 wherein said polypeptide comprises amino acids 1 to 289 of the sequence as set forth in SEQ ID NO. 2 or a conservatively substituted variant thereof.

21. The polypeptide according to claim 14 wherein said polypeptide comprises amino acids 1 to 291 of the sequence as set forth in SEQ ID NO. 2 or a conservatively substituted variant thereof.

22. The polypeptide according to claim 14 wherein said polypeptide comprises amino acids 5 to 265 of the sequence as set forth in SEQ ID NO. 2 or a conservatively substituted variant thereof.

23. The polypeptide according to claim 14 wherein said polypeptide comprises amino acids 5 to 289 of the sequence as set forth in SEQ ID NO. 2 or a conservatively substituted variant thereof.

24. The polypeptide according to claim 14 wherein said polypeptide comprises amino acids 5 to 291 of the sequence

as set forth in SEQ ID NO. 2 or a conservatively substituted variant thereof.

25. An expression vector for producing active human Chk1 kinase in a host cell, which vector comprises: a polynucleotide encoding active form of the human Chk1 kinase or an active human Chk1 kinase analog thereof; transcriptional and translational regulatory sequences functional in said host cell operably linked to said human Chk1 kinase-encoding polynucleotide; and a selectable marker.

26. The vector according to claim 25 wherein said polynucleotide encodes the active human Chk1 kinase, said active kinase comprising bases 35 to 830 of SEQ ID NO. 1.

27. The vector according to claim 25 wherein said vector is selected from the group consisting of pET28a, pAcSG2, and pFastBac.

28. The vector according to claim 25 wherein said vector is pFastBac-Nde.

29. The vector according to claim 25 wherein said selectable marker is selected from the group consisting of beta galactosidase, green fluorescent protein, and luciferase.

30. A host cell stably transformed and transfected with a polynucleotide encoding active form of the human Chk1 kinase or an active human Chk1 kinase analog thereof in a manner allowing the expression in said host cell of the human Chk1 kinase.

31. The host cell according to claim 30, wherein said polynucleotide encodes the active hChk1 kinase, said active kinase comprising bases 35 to 830 of SEQ ID NO. 1.

32. The host cell according to claim 30 wherein said host is *E. coli*.

33. The host cell according to claim 30 wherein said host is a recombinant baculovirus.

34. The host cell according to claim 30 wherein said host is an insect cell.

35. The host cell according to claim 34 wherein said insect cell is Sf9.

36. The host cell according to claim 30 wherein said host cell is transformed and transfected with said polynucleotide via an expression vector comprising said polynucleotide; a transcriptional and translational regulatory sequences functional in said host cell operably linked to said hChk1 kinase-encoding polynucleotide; and a selectable marker.

37. The host cell according to claim 36 wherein said expression vector is selected from the group consisting of pET28a, pAcSG2, and pFastBac.

38. The host cell according to claim 36 wherein said expression vector is pFastBac-Nde.

39. The host cell according to claim 36 wherein said selectable marker is selected from the group consisting of beta galactosidase, green fluorescent protein, and luciferase.

40. A method for assaying a candidate compound for its ability to interact with the human Chk1 comprising:

(a) expressing an isolated DNA sequence or variants thereof encoding the kinase domain of said human Chk1 in a host capable of producing said kinase in the catalytically active configuration, said kinase in a form which may be assayed for interaction of said kinase with said candidate compound;
(b) exposing said kinase to said candidate compound; and
(c) evaluating the interaction of said kinase with said candidate compound.

41. A method of identifying a Chk1 kinase inhibitor by determining the binding interactions between an organic compound and the binding site of the Chk1 kinase in the active conformation, said binding sites being defined by the crystal coordinates of provided in Figure 11, said method comprising:

(a) generating the binding cavity defined by the binding site on a computer screen;

(b) generating compounds with their spatial structure; and

(c) testing to see whether the compounds bind to at the Chk1 binding site; wherein those compounds that do bind to the Chk1 binding site can be identified as Chk1 inhibitors.

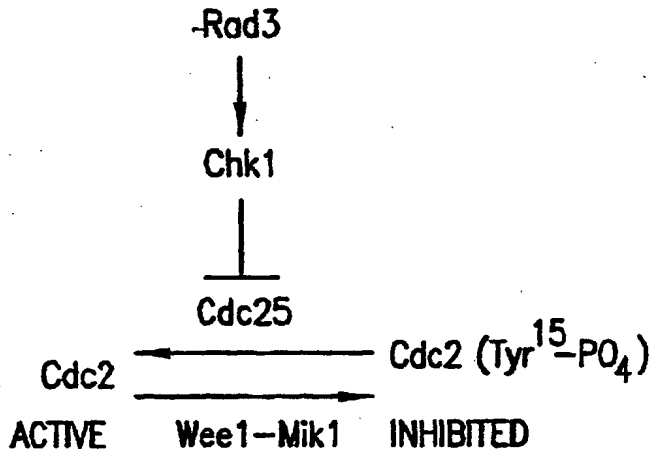


FIG.1

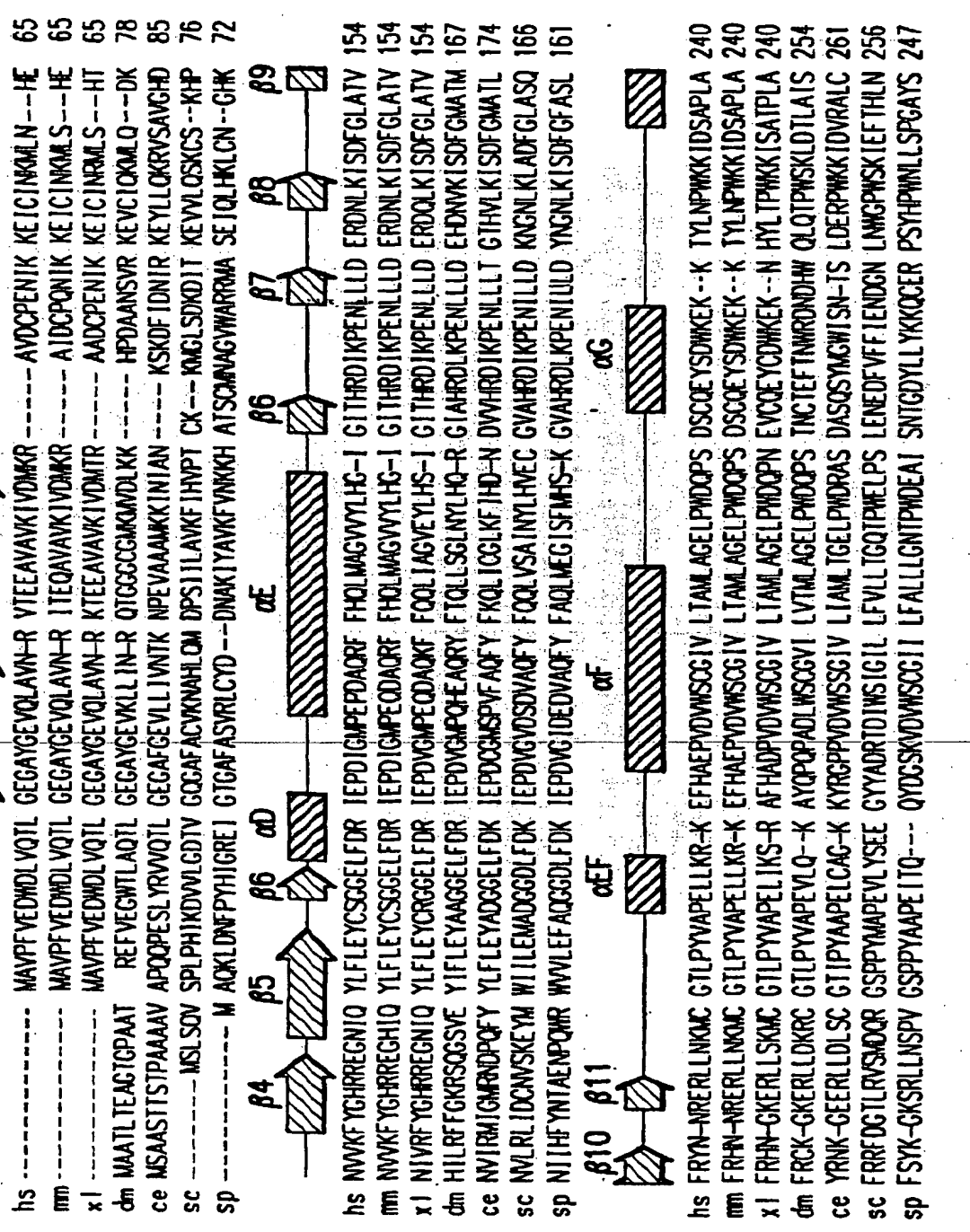


FIG.2A

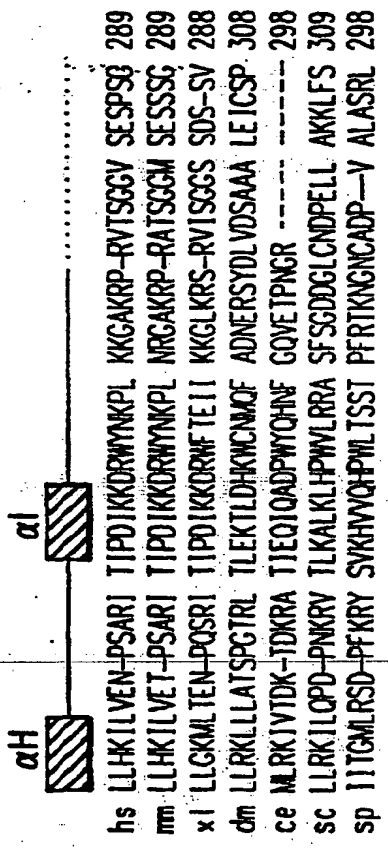


FIG.2B

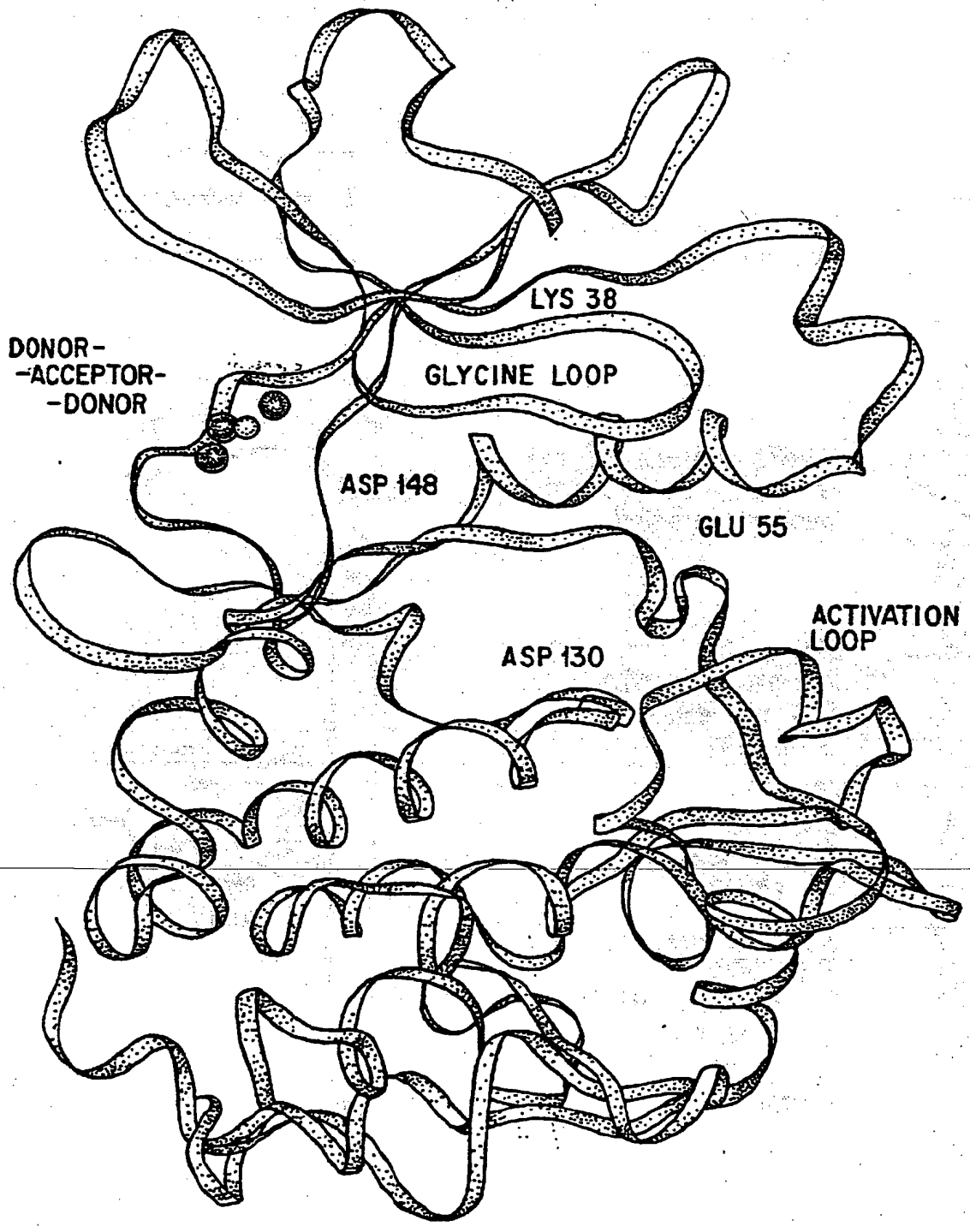

LYS 38
DONOR-
-ACCEPTOR-
-DONOR
GLYCINE LOOP
ASP 148
GLU 55
ACTIVATION
LOOP
ASP 130

FIG. 3

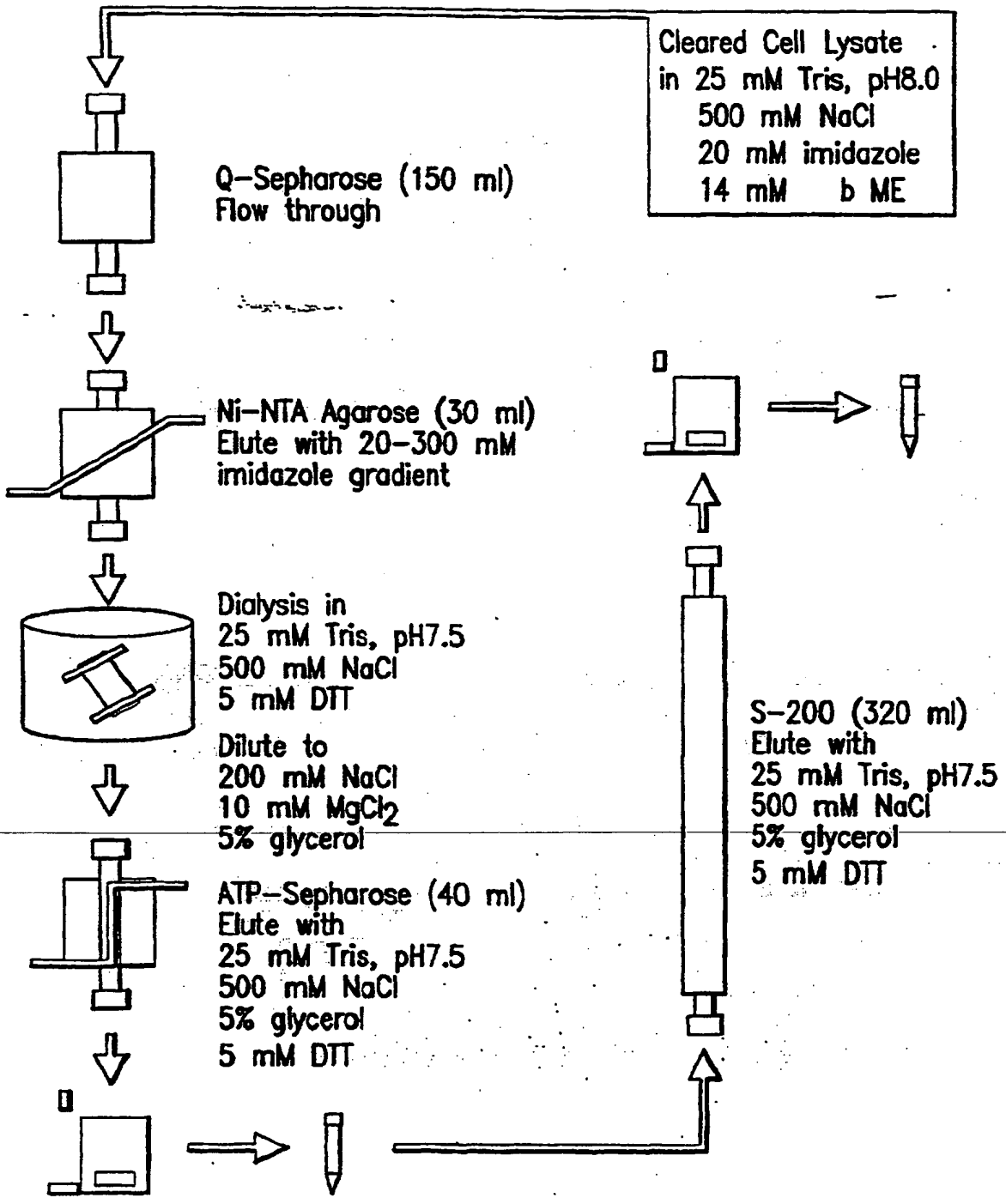


FIG.4

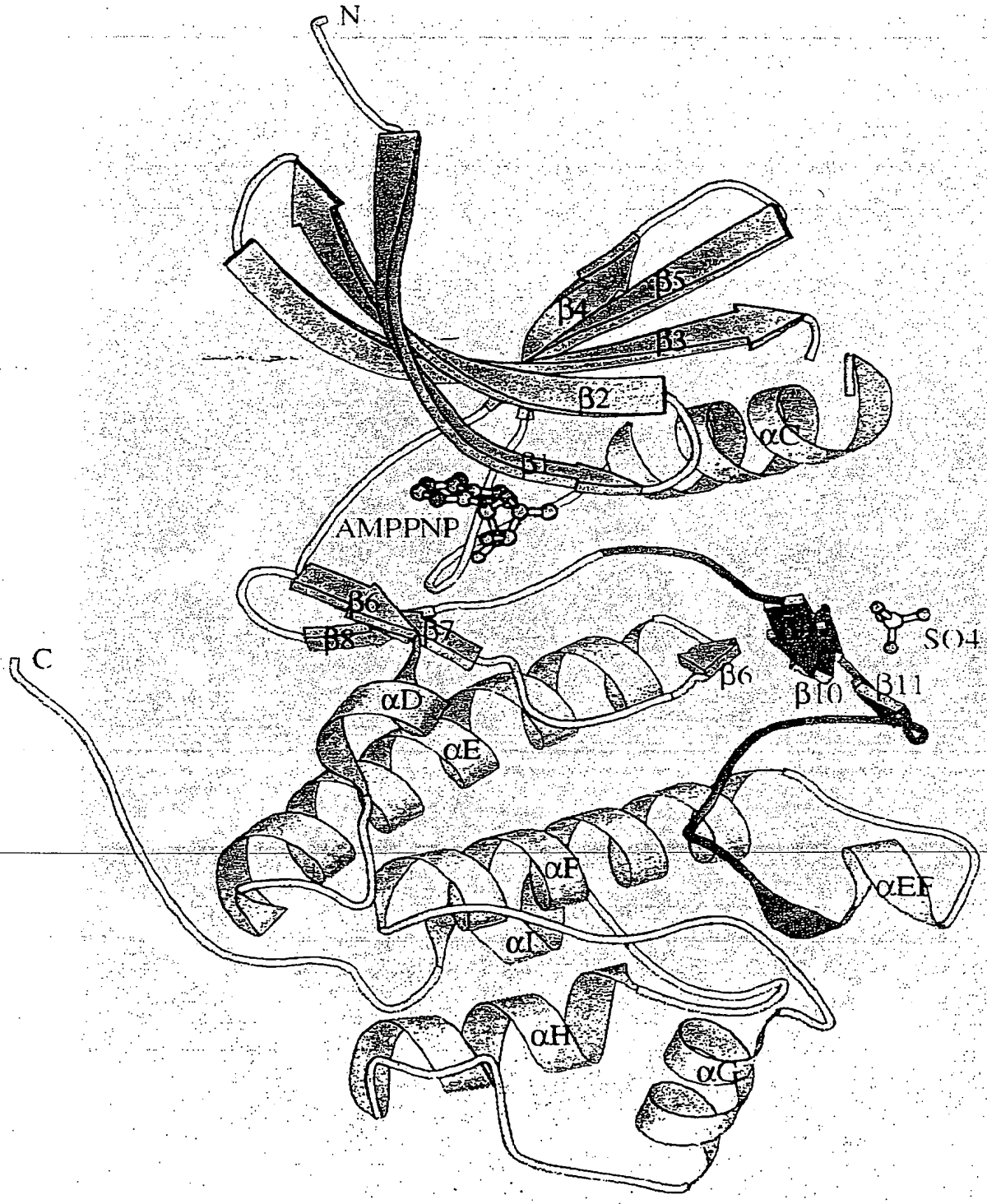

N
β5
β4
β3
β2
αC
β1
AMPPNP
β6
β8
β7
SO4
C
αD
β6
β10
β11
αE
αF
αEF
αI
αH
αG

FIG.5

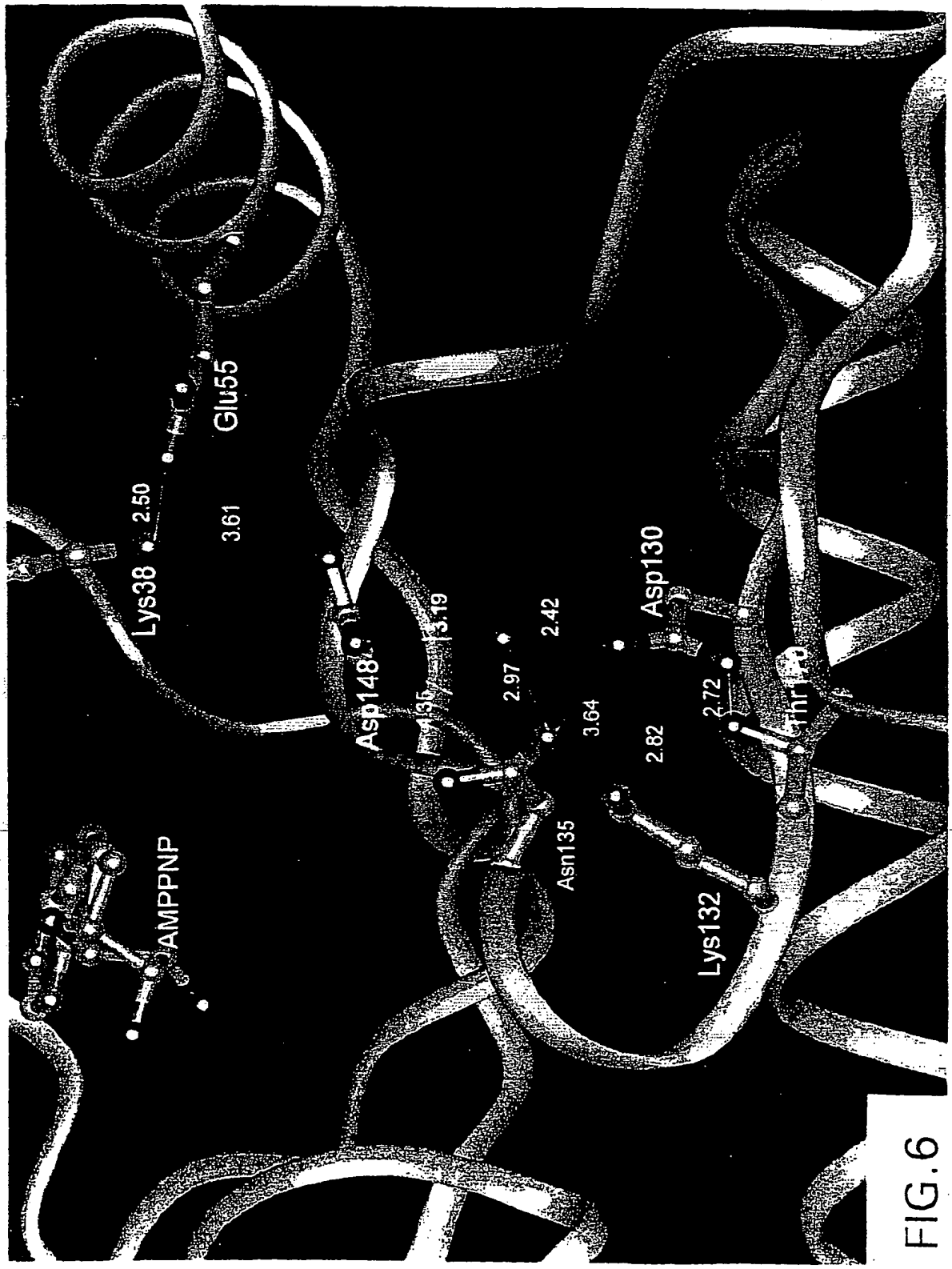


FIG.6

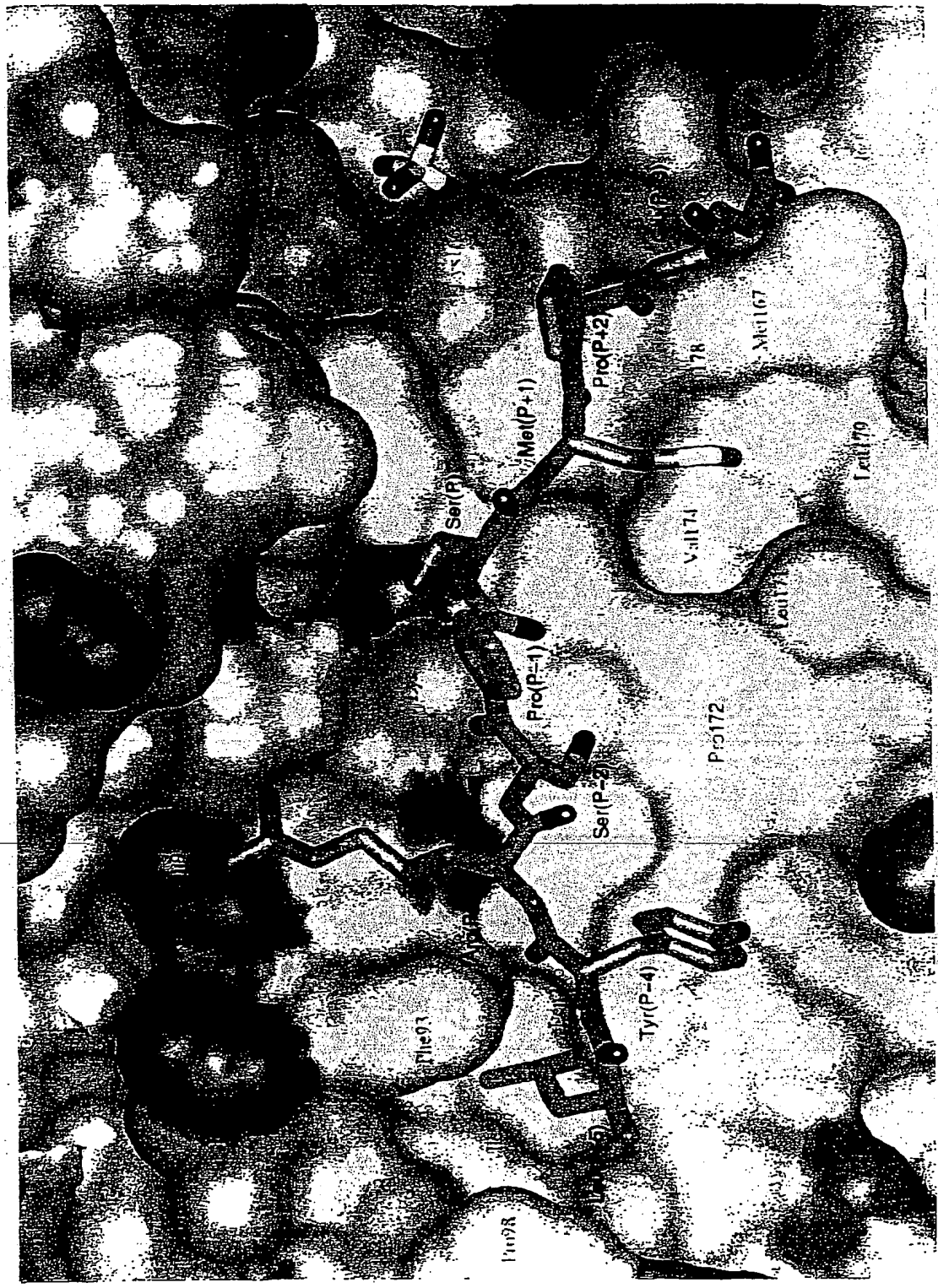

Ser(P)
Met(P+1)
Pro(P+2)
Pro(P-1)
Ser(P-2)
Tyr(P-4)
Val174
Pro172
Leu179
Met167

FIG.7

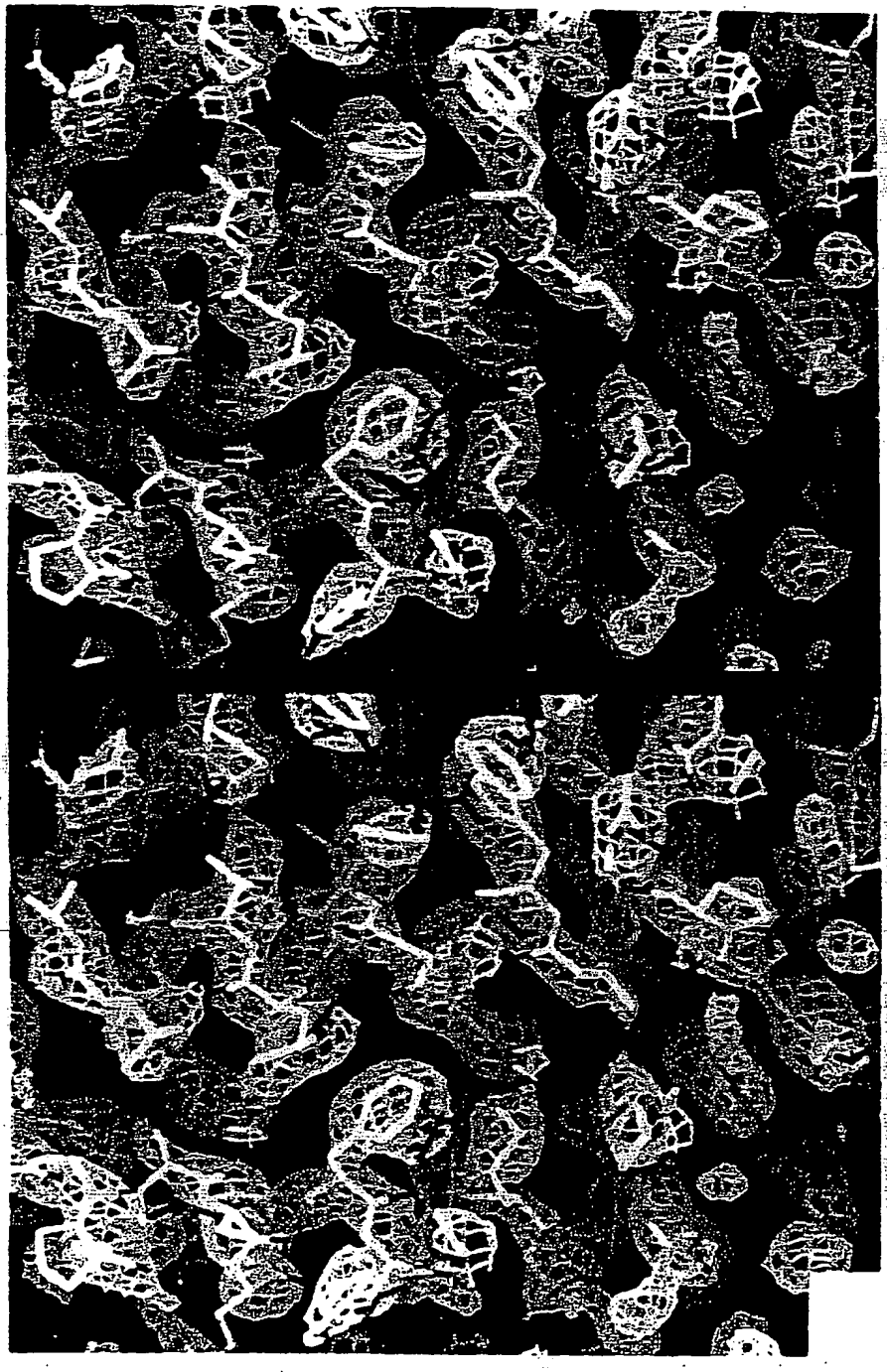


FIG.8A

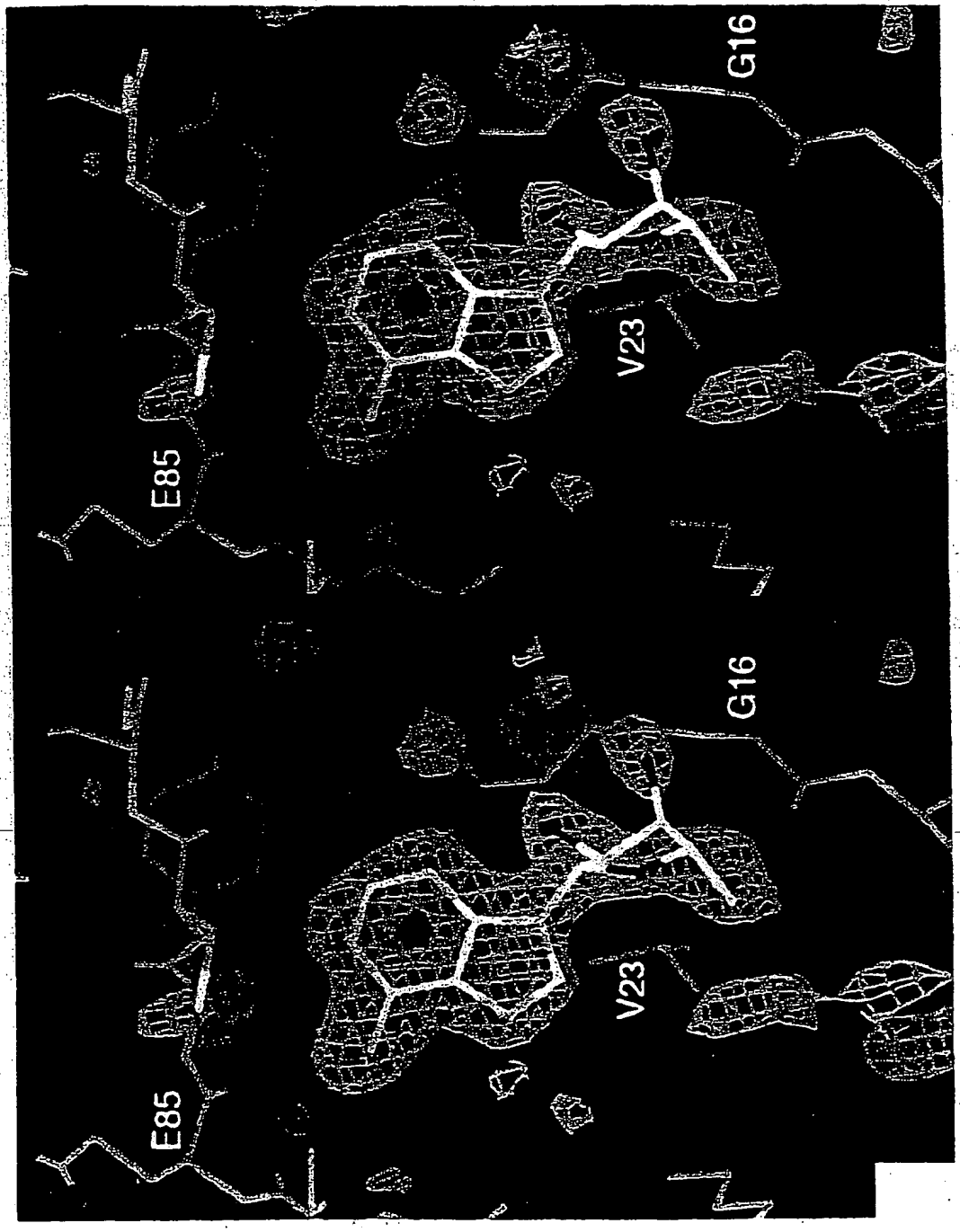


FIG.8B

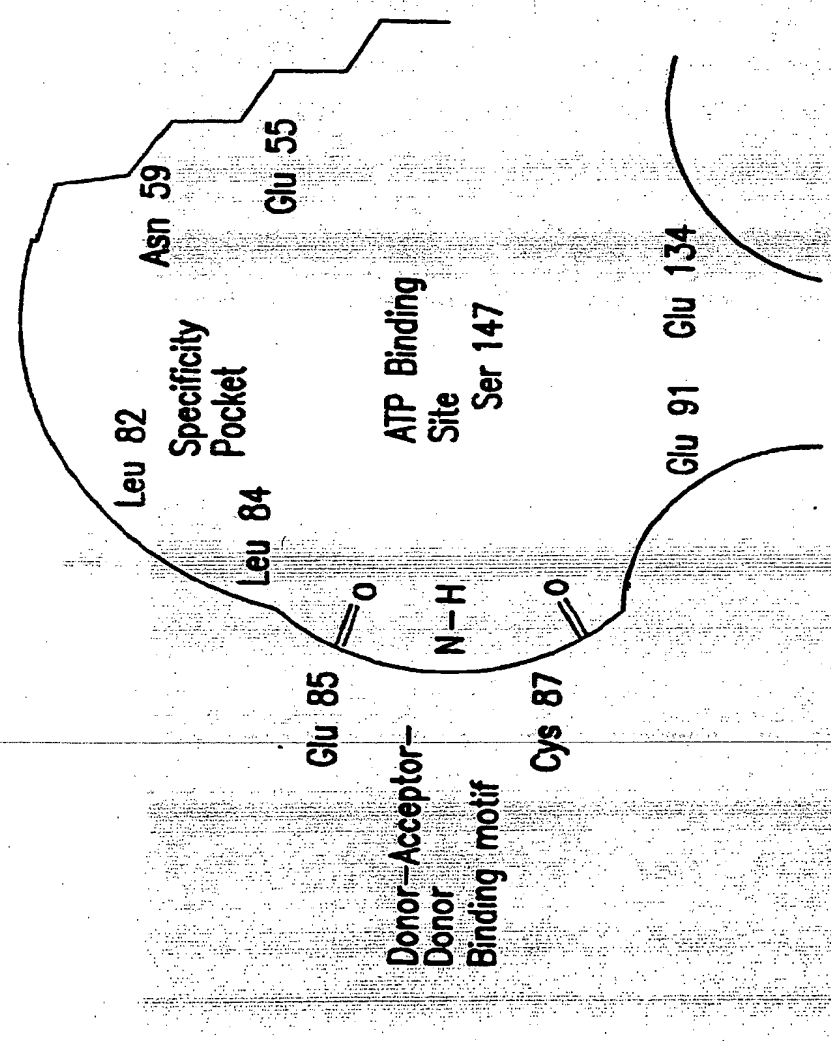
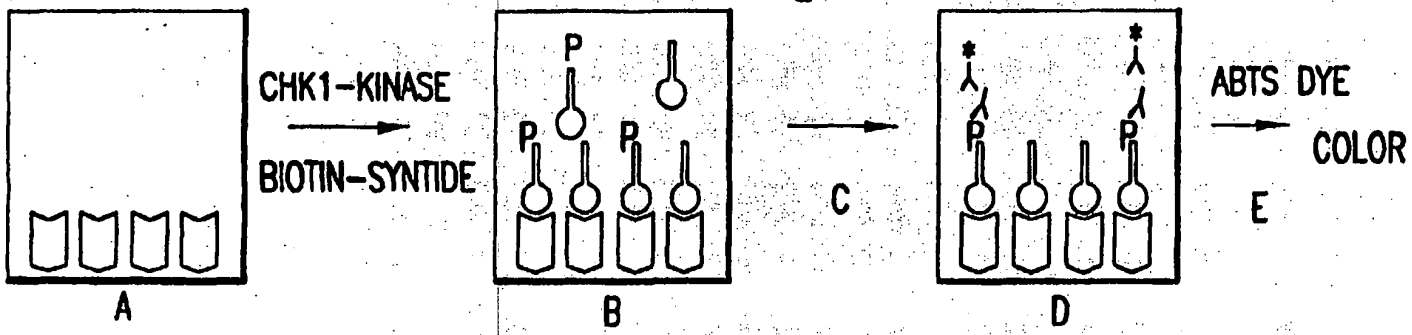


FIG.9

CHK1 KINASE HTS ELISA

10nM CHK1 (KH289 KINASE DOMAIN)

BIOTIN-SYNTIDE (10μM)+ATP (50μM) $\xrightleftharpoons[MgCl_2]{}$ BIOTIN-SYNTIDE (Ser-PO_3) + ADP



STEPS A AND B

CONDUCT KINASE REACTION IN NEUTRAVIDIN COATED 96-WELL PLATES FOR 10min.

STEPS C AND D

WASH PLATES, THEN INCUBATE WITH RABBIT-ANTI-PHOSPHOSYNTIDE ANTIBODY FOR 60 min. WASH PLATES, INCUBATE WITH GOAT ANTI-Rb-IgG-HRP.

STEP E

WASH PLATES, THEN ADD ABTS DYE, READ O.D. (405nm)IN A 96-WELL PLATE READER.

NEUTRAVIDIN
BIOTIN-SYNTIDE
P BIOTIN-SYNTIDE (Ser-PO_3)
Rb-ANTI-PHOSPHOSYNTIDE Ab
Gt ANTI-Rb-IgG-HRP

FIG.10

ATOM	1	CB	ALA	2	0.113	10.279	-12.669	1.00	55.20
ATOM	2	C	ALA	2	0.954	8.071	-13.488	1.00	54.08
ATOM	3	O	ALA	2	0.890	7.468	-14.560	1.00	54.24
ATOM	4	N	ALA	2	-0.778	8.182	-11.709	1.00	57.23
ATOM	5	CA	ALA	2	-0.258	8.824	-12.949	1.00	55.69
ATOM	6	N	VAL	3	2.056	8.107	-12.740	1.00	51.32
ATOM	7	CA	VAL	3	3.284	7.427	-13.149	1.00	47.11
ATOM	8	CB	VAL	3	4.508	7.949	-12.363	1.00	46.10
ATOM	9	CG1	VAL	3	5.794	7.398	-12.973	1.00	41.34
ATOM	10	CG2	VAL	3	4.524	9.467	-12.367	1.00	48.87
ATOM	11	C	VAL	3	3.143	5.920	-12.922	1.00	44.85
ATOM	12	O	VAL	3	2.969	5.461	-11.795	1.00	45.58
ATOM	13	N	PRO	4	3.231	5.132	-14.003	1.00	41.89
ATOM	14	CD	PRO	4	3.546	5.613	-15.363	1.00	37.40
ATOM	15	CA	PRO	4	3.112	3.672	-13.991	1.00	41.11
ATOM	16	CB	PRO	4	3.743	3.276	-15.323	1.00	34.82
ATOM	17	CG	PRO	4	3.281	4.388	-16.215	1.00	31.95
ATOM	18	C	PRO	4	3.667	2.858	-12.815	1.00	42.75
ATOM	19	O	PRO	4	2.936	2.534	-11.875	1.00	47.35
ATOM	20	N	PHE	5	4.954	2.540	-12.869	1.00	40.95
ATOM	21	CA	PHE	5	5.591	1.699	-11.856	1.00	40.30
ATOM	22	CB	PHE	5	6.705	0.882	-12.522	1.00	36.35
ATOM	23	CG	PHE	5	6.572	0.770	-14.020	1.00	32.27
ATOM	24	CD1	PHE	5	7.335	1.578	-14.862	1.00	27.57
ATOM	25	CD2	PHE	5	5.702	-0.154	-14.589	1.00	32.16
ATOM	26	CE1	PHE	5	7.237	1.465	-16.248	1.00	27.10
ATOM	27	CE2	PHE	5	5.593	-0.276	-15.979	1.00	30.91
ATOM	28	CZ	PHE	5	6.363	0.535	-16.809	1.00	28.05
ATOM	29	C	PHE	5	6.156	2.348	-10.589	1.00	39.99
ATOM	30	O	PHE	5	7.191	1.908	-10.088	1.00	38.49
ATOM	31	N	VAL	6	5.486	3.360	-10.048	1.00	40.37
ATOM	32	CA	VAL	6	5.994	4.011	-8.842	1.00	40.35
ATOM	33	CB	VAL	6	5.424	5.437	-8.690	1.00	42.42
ATOM	34	CG1	VAL	6	6.135	6.169	-7.563	1.00	45.17
ATOM	35	CG2	VAL	6	5.593	6.194	-9.980	1.00	43.26
ATOM	36	C	VAL	6	5.676	3.219	-7.573	1.00	39.11
ATOM	37	O	VAL	6	6.229	3.492	-6.507	1.00	38.75
ATOM	38	N	GLU	7	4.796	2.232	-7.693	1.00	36.63
ATOM	39	CA	GLU	7	4.408	1.411	-6.550	1.00	34.52
ATOM	40	CB	GLU	7	2.931	1.035	-6.659	1.00	41.81
ATOM	41	CG	GLU	7	1.981	2.219	-6.618	1.00	51.32
ATOM	42	CD	GLU	7	1.963	2.906	-5.267	1.00	60.70

FIG.11A-1

ATOM	43	OE1	GLU	7	3.021	3.416	-4.840	1.00	63.96
ATOM	44	OE2	GLU	7	0.888	2.935	-4.631	1.00	70.24
ATOM	45	C	GLU	7	5.246	0.141	-6.443	1.00	31.93
ATOM	46	O	GLU	7	5.036	-0.675	-5.544	1.00	32.27
ATOM	47	N	ASP	8	6.193	-0.024	-7.360	1.00	31.04
ATOM	48	CA	ASP	8	7.052	-1.204	-7.367	1.00	31.42
ATOM	49	CB	ASP	8	7.404	-1.597	-8.805	1.00	35.69
ATOM	50	CG	ASP	8	6.202	-2.095	-9.586	1.00	44.50
ATOM	51	OD1	ASP	8	5.534	-3.039	-9.115	1.00	46.19
ATOM	52	OD2	ASP	8	5.929	-1.544	-10.673	1.00	49.49
ATOM	53	C	ASP	8	8.338	-1.002	-6.576	1.00	31.44
ATOM	54	O	ASP	8	9.039	-0.003	-6.749	1.00	32.04
ATOM	55	N	TRP	9	8.644	-1.972	-5.720	1.00	30.97
ATOM	56	CA	TRP	9	9.837	-1.939	-4.883	1.00	31.19
ATOM	57	CB	TRP	9	9.435	-1.779	-3.408	1.00	32.92
ATOM	58	CG	TRP	9	9.527	-0.371	-2.877	1.00	37.61
ATOM	59	CD2	TRP	9	8.464	0.583	-2.781	1.00	34.10
ATOM	60	CE2	TRP	9	9.014	1.770	-2.242	1.00	35.49
ATOM	61	CE3	TRP	9	7.100	0.554	-3.100	1.00	28.78
ATOM	62	CD1	TRP	9	10.648	0.258	-2.404	1.00	37.08
ATOM	63	NE1	TRP	9	10.347	1.543	-2.020	1.00	32.55
ATOM	64	CZ2	TRP	9	8.247	2.916	-2.015	1.00	34.87
ATOM	65	CZ3	TRP	9	6.337	1.693	-2.876	1.00	36.67
ATOM	66	CH2	TRP	9	6.914	2.860	-2.338	1.00	40.32
ATOM	67	C	TRP	9	10.666	-3.213	-5.044	1.00	31.47
ATOM	68	O	TRP	9	10.127	-4.320	-5.057	1.00	32.63
ATOM	69	N	ASP	10	11.977	-3.046	-5.173	1.00	30.81
ATOM	70	CA	ASP	10	12.893	-4.173	-5.304	1.00	30.35
ATOM	71	CB	ASP	10	13.994	-3.849	-6.316	1.00	31.71
ATOM	72	CG	ASP	10	13.474	-3.745	-7.736	1.00	35.37
ATOM	73	OD1	ASP	10	14.061	-2.971	-8.524	1.00	41.94
ATOM	74	OD2	ASP	10	12.495	-4.445	-8.069	1.00	34.42
ATOM	75	C	ASP	10	13.539	-4.444	-3.945	1.00	30.57
ATOM	76	O	ASP	10	14.029	-3.521	-3.290	1.00	27.52
ATOM	77	N	LEU	11	13.535	-5.703	-3.522	1.00	32.48
ATOM	78	CA	LEU	11	14.148	-6.078	-2.249	1.00	36.27
ATOM	79	CB	LEU	11	13.432	-7.290	-1.645	1.00	37.99
ATOM	80	CG	LEU	11	11.990	-7.058	-1.182	1.00	39.05
ATOM	81	CD1	LEU	11	11.125	-6.630	-2.357	1.00	40.90
ATOM	82	CD2	LEU	11	11.442	-8.335	-0.563	1.00	43.43
ATOM	83	C	LEU	11	15.609	-6.405	-2.537	1.00	38.60
ATOM	84	O	LEU	11	15.934	-7.508	-2.975	1.00	38.62

FIG.11A-2

ATOM	85	N	VAL	12	16.480	-5.432	-2.287	1.00	41.77
ATOM	86	CA	VAL	12	17.909	-5.563	-2.557	1.00	44.63
ATOM	87	CB	VAL	12	18.555	-4.169	-2.720	1.00	45.32
ATOM	88	CG1	VAL	12	20.017	-4.310	-3.124	1.00	51.19
ATOM	89	CG2	VAL	12	17.788	-3.365	-3.757	1.00	42.65
ATOM	90	C	VAL	12	18.739	-6.353	-1.549	1.00	46.95
ATOM	91	O	VAL	12	19.663	-7.068	-1.937	1.00	47.15
ATOM	92	N	GLN	13	18.431	-6.223	-0.262	1.00	47.33
ATOM	93	CA	GLN	13	19.195	-6.940	0.752	1.00	47.97
ATOM	94	CB	GLN	13	20.558	-6.275	0.948	1.00	49.67
ATOM	95	CG	GLN	13	20.482	-4.801	1.303	1.00	53.58
ATOM	96	CD	GLN	13	21.833	-4.223	1.675	1.00	55.37
ATOM	97	OE1	GLN	13	22.410	-4.578	2.703	1.00	56.20
ATOM	98	NE2	GLN	13	22.347	-3.329	0.836	1.00	58.05
ATOM	99	C	GLN	13	18.505	-7.055	2.104	1.00	48.35
ATOM	100	O	GLN	13	17.636	-6.255	2.452	1.00	47.74
ATOM	101	N	THR	14	18.916	-8.063	2.866	1.00	48.79
ATOM	102	CA	THR	14	18.365	-8.310	4.192	1.00	49.84
ATOM	103	CB	THR	14	18.497	-9.795	4.575	1.00	51.16
ATOM	104	OG1	THR	14	18.202	-9.961	5.968	1.00	53.80
ATOM	105	CG2	THR	14	19.907	-10.293	4.293	1.00	55.63
ATOM	106	C	THR	14	19.106	-7.478	5.229	1.00	49.90
ATOM	107	O	THR	14	20.334	-7.512	5.293	1.00	51.70
ATOM	108	N	LEU	15	18.363	-6.726	6.034	1.00	48.90
ATOM	109	CA	LEU	15	18.977	-5.903	7.067	1.00	49.63
ATOM	110	CB	LEU	15	18.139	-4.650	7.344	1.00	44.87
ATOM	111	CG	LEU	15	17.959	-3.650	6.203	1.00	39.00
ATOM	112	CD1	LEU	15	19.307	-3.313	5.581	1.00	32.83
ATOM	113	CD2	LEU	15	17.039	-4.247	5.172	1.00	41.59
ATOM	114	C	LEU	15	19.120	-6.706	8.349	1.00	51.59
ATOM	115	O	LEU	15	20.050	-6.493	9.126	1.00	51.40
ATOM	116	N	GLY	16	18.191	-7.631	8.562	1.00	53.10
ATOM	117	CA	GLY	16	18.227	-8.458	9.752	1.00	55.79
ATOM	118	C	GLY	16	17.043	-9.401	9.824	1.00	58.51
ATOM	119	O	GLY	16	15.909	-9.008	9.550	1.00	58.89
ATOM	120	N	GLU	17	17.307	-10.651	10.191	1.00	60.68
ATOM	121	CA	GLU	17	16.257	-11.655	10.301	1.00	63.27
ATOM	122	CB	GLU	17	16.703	-12.961	9.644	1.00	67.17
ATOM	123	CG	GLU	17	16.978	-12.845	8.156	1.00	69.72
ATOM	124	CD	GLU	17	17.430	-14.155	7.548	1.00	74.27
ATOM	125	OE1	GLU	17	18.488	-14.672	7.965	1.00	77.30
ATOM	126	OE2	GLU	17	16.727	-14.670	6.653	1.00	75.48

FIG.11A-3

ATOM	127	C	GLU	17	15.914	-11.911	11.762	1.00 64.57
ATOM	128	O	GLU	17	16.591	-12.682	12.441	1.00 63.90
ATOM	129	N	GLY	18	14.859	-11.258	12.238	1.00 66.47
ATOM	130	CA	GLY	18	14.445	-11.429	13.618	1.00 66.94
ATOM	131	C	GLY	18	13.834	-12.793	13.870	1.00 67.94
ATOM	132	O	GLY	18	13.610	-13.565	12.936	1.00 68.20
ATOM	133	N	ALA	19	13.565	-13.093	15.137	1.00 68.69
ATOM	134	CA	ALA	19	12.973	-14.370	15.512	1.00 67.96
ATOM	135	CB	ALA	19	13.110	-14.586	17.015	1.00 67.41
ATOM	136	C	ALA	19	11.504	-14.412	15.107	1.00 67.21
ATOM	137	O	ALA	19	10.812	-15.403	15.346	1.00 67.90
ATOM	138	N	TYR	20	11.035	-13.330	14.493	1.00 66.16
ATOM	139	CA	TYR	20	9.648	-13.236	14.052	1.00 65.86
ATOM	140	CB	TYR	20	8.813	-12.492	15.101	1.00 66.27
ATOM	141	CG	TYR	20	9.495	-11.278	15.697	1.00 68.01
ATOM	142	CD1	TYR	20	9.896	-10.210	14.894	1.00 72.07
ATOM	143	CE1	TYR	20	10.528	-9.093	15.442	1.00 72.81
ATOM	144	CD2	TYR	20	9.743	-11.201	17.068	1.00 64.75
ATOM	145	CE2	TYR	20	10.373	-10.090	17.625	1.00 66.10
ATOM	146	CZ	TYR	20	10.762	-9.041	16.806	1.00 71.06
ATOM	147	OH	TYR	20	11.385	-7.942	17.352	1.00 74.54
ATOM	148	C	TYR	20	9.522	-12.549	12.693	1.00 64.83
ATOM	149	O	TYR	20	8.770	-11.586	12.536	1.00 63.94
ATOM	150	N	GLY	21	10.261	-13.058	11.712	1.00 63.95
ATOM	151	CA	GLY	21	10.222	-12.488	10.378	1.00 62.81
ATOM	152	C	GLY	21	11.583	-12.006	9.915	1.00 61.39
ATOM	153	O	GLY	21	12.616	-12.527	10.341	1.00 61.10
ATOM	154	N	GLU	22	11.587	-11.008	9.038	1.00 58.87
ATOM	155	CA	GLU	22	12.831	-10.455	8.518	1.00 55.14
ATOM	156	CB	GLU	22	13.362	-11.322	7.373	1.00 58.20
ATOM	157	CG	GLU	22	12.435	-11.395	6.170	1.00 64.23
ATOM	158	CD	GLU	22	13.021	-12.200	5.027	1.00 70.83
ATOM	159	OE1	GLU	22	12.352	-12.322	3.979	1.00 70.63
ATOM	160	OE2	GLU	22	14.152	-12.711	5.174	1.00 75.29
ATOM	161	C	GLU	22	12.620	-9.032	8.018	1.00 49.83
ATOM	162	O	GLU	22	11.492	-8.610	7.773	1.00 48.81
ATOM	163	N	VAL	23	13.716	-8.296	7.875	1.00 47.61
ATOM	164	CA	VAL	23	13.656	-6.925	7.393	1.00 44.26
ATOM	165	CB	VAL	23	14.211	-5.937	8.441	1.00 43.86
ATOM	166	CG1	VAL	23	14.076	-4.512	7.935	1.00 42.93
ATOM	167	CG2	VAL	23	13.469	-6.107	9.756	1.00 40.58
ATOM	168	C	VAL	23	14.479	-6.819	6.117	1.00 40.96

FIG.11A-4

ATOM	169	O	VAL	23	15.651	-7.190	6.091	1.00	38.29
ATOM	170	N	GLN	24	13.853	-6.322	5.057	1.00	40.99
ATOM	171	CA	GLN	24	14.518	-6.172	3.770	1.00	40.30
ATOM	172	CB	GLN	24	13.749	-6.938	2.689	1.00	41.52
ATOM	173	CG	GLN	24	13.812	-8.450	2.813	1.00	47.92
ATOM	174	CD	GLN	24	15.194	-8.999	2.527	1.00	55.67
ATOM	175	OE1	GLN	24	15.789	-8.701	1.490	1.00	59.08
ATOM	176	NE2	GLN	24	15.712	-9.810	3.442	1.00	59.81
ATOM	177	C	GLN	24	14.634	-4.711	3.353	1.00	39.30
ATOM	178	O	GLN	24	13.757	-3.896	3.643	1.00	37.62
ATOM	179	N	LEU	25	15.733	-4.387	2.680	1.00	38.08
ATOM	180	CA	LEU	25	15.952	-3.036	2.189	1.00	36.35
ATOM	181	CB	LEU	25	17.449	-2.765	2.017	1.00	33.98
ATOM	182	CG	LEU	25	17.903	-1.405	1.474	1.00	34.17
ATOM	183	CD1	LEU	25	17.676	-1.327	-0.018	1.00	37.28
ATOM	184	CD2	LEU	25	17.159	-0.293	2.191	1.00	37.37
ATOM	185	C	LEU	25	15.245	-2.983	0.843	1.00	34.98
ATOM	186	O	LEU	25	15.589	-3.731	-0.072	1.00	34.14
ATOM	187	N	ALA	26	14.249	-2.111	0.733	1.00	33.58
ATOM	188	CA	ALA	26	13.485	-1.976	-0.501	1.00	32.06
ATOM	189	CB	ALA	26	11.996	-2.034	-0.195	1.00	31.61
ATOM	190	C	ALA	26	13.816	-0.682	-1.229	1.00	30.85
ATOM	191	O	ALA	26	13.860	0.386	-0.624	1.00	30.61
ATOM	192	N	VAL	27	14.047	-0.788	-2.535	1.00	29.88
ATOM	193	CA	VAL	27	14.366	0.373	-3.353	1.00	28.11
ATOM	194	CB	VAL	27	15.735	0.207	-4.046	1.00	25.40
ATOM	195	CG1	VAL	27	16.053	1.442	-4.877	1.00	23.89
ATOM	196	CG2	VAL	27	16.818	-0.016	-2.997	1.00	24.52
ATOM	197	C	VAL	27	13.277	0.540	-4.404	1.00	25.70
ATOM	198	O	VAL	27	12.933	-0.409	-5.112	1.00	26.38
ATOM	199	N	ASN	28	12.724	1.745	-4.493	1.00	23.90
ATOM	200	CA	ASN	28	11.657	2.014	-5.444	1.00	23.36
ATOM	201	CB	ASN	28	11.047	3.391	-5.185	1.00	22.07
ATOM	202	CG	ASN	28	9.822	3.652	-6.030	1.00	23.58
ATOM	203	OD1	ASN	28	9.925	4.068	-7.187	1.00	23.59
ATOM	204	ND2	ASN	28	8.648	3.396	-5.462	1.00	27.10
ATOM	205	C	ASN	28	12.169	1.926	-6.872	1.00	23.17
ATOM	206	O	ASN	28	13.204	2.493	-7.212	1.00	21.97
ATOM	207	N	ARG	29	11.427	1.197	-7.693	1.00	25.26
ATOM	208	CA	ARG	29	11.771	0.981	-9.094	1.00	25.06
ATOM	209	CB	ARG	29	10.695	0.099	-9.728	1.00	24.87
ATOM	210	CG	ARG	29	10.782	-0.044	-11.235	1.00	22.45

FIG.11A-5

ATOM	211	CD	ARG	29	9.652	-0.930	-11.737	1.00	20.20
ATOM	212	NE	ARG	29	9.593	-0.954	-13.198	1.00	19.85
ATOM	213	CZ	ARG	29	8.731	-1.680	-13.901	1.00	21.65
ATOM	214	NH1	ARG	29	7.847	-2.449	-13.281	1.00	26.57
ATOM	215	NH2	ARG	29	8.756	-1.642	-15.227	1.00	23.50
ATOM	216	C	ARG	29	11.938	2.269	-9.901	1.00	25.06
ATOM	217	O	ARG	29	12.784	2.347	-10.799	1.00	25.77
ATOM	218	N	VAL	30	11.136	3.277	-9.576	1.00	23.54
ATOM	219	CA	VAL	30	11.178	4.548	-10.291	1.00	22.97
ATOM	220	CB	VAL	30	9.753	5.109	-10.499	1.00	22.15
ATOM	221	CG1	VAL	30	9.824	6.517	-11.081	1.00	23.25
ATOM	222	CG2	VAL	30	8.956	4.190	-11.413	1.00	20.64
ATOM	223	C	VAL	30	12.014	5.635	-9.623	1.00	24.22
ATOM	224	O	VAL	30	12.907	6.210	-10.244	1.00	24.96
ATOM	225	N	THR	31	11.724	5.915	-8.355	1.00	25.29
ATOM	226	CA	THR	31	12.427	6.970	-7.633	1.00	25.85
ATOM	227	CB	THR	31	11.537	7.554	-6.528	1.00	29.34
ATOM	228	OG1	THR	31	11.357	6.574	-5.498	1.00	30.34
ATOM	229	CG2	THR	31	10.177	7.945	-7.093	1.00	32.37
ATOM	230	C	THR	31	13.742	6.557	-6.989	1.00	25.05
ATOM	231	O	THR	31	14.588	7.405	-6.695	1.00	24.93
ATOM	232	N	GLU	32	13.901	5.256	-6.771	1.00	23.56
ATOM	233	CA	GLU	32	15.088	4.702	-6.136	1.00	25.89
ATOM	234	CB	GLU	32	16.360	5.169	-6.855	1.00	31.18
ATOM	235	CG	GLU	32	16.441	4.626	-8.275	1.00	36.10
ATOM	236	CD	GLU	32	17.781	4.857	-8.928	1.00	40.49
ATOM	237	OE1	GLU	32	18.800	4.385	-8.381	1.00	47.18
ATOM	238	OE2	GLU	32	17.812	5.505	-9.992	1.00	34.21
ATOM	239	C	GLU	32	15.125	5.060	-4.653	1.00	28.39
ATOM	240	O	GLU	32	16.155	4.935	-3.992	1.00	28.96
ATOM	241	N	GLU	33	13.985	5.506	-4.140	1.00	29.00
ATOM	242	CA	GLU	33	13.876	5.833	-2.722	1.00	30.79
ATOM	243	CB	GLU	33	12.483	6.375	-2.395	1.00	31.20
ATOM	244	CG	GLU	33	12.198	6.452	-0.897	1.00	47.15
ATOM	245	CD	GLU	33	10.798	6.945	-0.577	1.00	57.42
ATOM	246	OE1	GLU	33	9.828	6.400	-1.144	1.00	63.55
ATOM	247	OE2	GLU	33	10.666	7.871	0.252	1.00	63.48
ATOM	248	C	GLU	33	14.101	4.527	-1.971	1.00	28.96
ATOM	249	O	GLU	33	13.613	3.476	-2.391	1.00	28.97
ATOM	250	N	ALA	34	14.835	4.592	-0.864	1.00	28.98
ATOM	251	CA	ALA	34	15.115	3.403	-0.069	1.00	29.99
ATOM	252	CB	ALA	34	16.607	3.314	0.234	1.00	26.15

FIG. 11A-6

ATOM	253	C	ALA	34	14.319	3.410	1.230	1.00	32.79
ATOM	254	O	ALA	34	14.272	4.418	1.933	1.00	34.60
ATOM	255	N	VAL	35	13.685	2.281	1.530	1.00	31.99
ATOM	256	CA	VAL	35	12.901	2.132	2.750	1.00	32.37
ATOM	257	CB	VAL	35	11.388	2.327	2.497	1.00	32.24
ATOM	258	CG1	VAL	35	11.132	3.701	1.902	1.00	31.97
ATOM	259	CG2	VAL	35	10.866	1.230	1.579	1.00	32.80
ATOM	260	C	VAL	35	13.117	0.726	3.282	1.00	33.29
ATOM	261	O	VAL	35	13.609	-0.149	2.564	1.00	31.06
ATOM	262	N	ALA	36	12.759	0.513	4.543	1.00	32.66
ATOM	263	CA	ALA	36	12.902	-0.797	5.152	1.00	32.39
ATOM	264	CB	ALA	36	13.444	-0.669	6.577	1.00	30.92
ATOM	265	C	ALA	36	11.535	-1.462	5.166	1.00	32.53
ATOM	266	O	ALA	36	10.533	-0.845	5.532	1.00	29.98
ATOM	267	N	VAL	37	11.492	-2.720	4.749	1.00	34.45
ATOM	268	CA	VAL	37	10.240	-3.456	4.729	1.00	37.01
ATOM	269	CB	VAL	37	9.919	-3.981	3.316	1.00	39.07
ATOM	270	CG1	VAL	37	8.660	-4.841	3.352	1.00	41.91
ATOM	271	CG2	VAL	37	9.729	-2.810	2.366	1.00	40.40
ATOM	272	C	VAL	37	10.322	-4.629	5.690	1.00	37.16
ATOM	273	O	VAL	37	11.134	-5.534	5.514	1.00	36.61
ATOM	274	N	LYS	38	9.485	-4.592	6.720	1.00	37.96
ATOM	275	CA	LYS	38	9.451	-5.655	7.713	1.00	39.49
ATOM	276	CB	LYS	38	9.048	-5.086	9.077	1.00	38.70
ATOM	277	CG	LYS	38	9.168	-6.066	10.236	1.00	38.05
ATOM	278	CD	LYS	38	8.840	-5.378	11.554	1.00	40.91
ATOM	279	CE	LYS	38	9.022	-6.309	12.737	1.00	46.69
ATOM	280	NZ	LYS	38	8.790	-5.598	14.026	1.00	49.50
ATOM	281	C	LYS	38	8.434	-6.688	7.246	1.00	40.71
ATOM	282	O	LYS	38	7.253	-6.379	7.084	1.00	40.05
ATOM	283	N	ILE	39	8.901	-7.910	7.016	1.00	42.81
ATOM	284	CA	ILE	39	8.030	-8.983	6.553	1.00	45.99
ATOM	285	CB	ILE	39	8.666	-9.730	5.364	1.00	45.59
ATOM	286	CG2	ILE	39	7.693	-10.765	4.818	1.00	46.73
ATOM	287	CG1	ILE	39	9.046	-8.728	4.270	1.00	44.50
ATOM	288	CD1	ILE	39	9.742	-9.349	3.075	1.00	49.55
ATOM	289	C	ILE	39	7.753	-9.977	7.675	1.00	48.22
ATOM	290	O	ILE	39	8.673	-10.593	8.210	1.00	48.95
ATOM	291	N	VAL	40	6.480	-10.129	8.025	1.00	50.79
ATOM	292	CA	VAL	40	6.090	-11.046	9.089	1.00	53.10
ATOM	293	CB	VAL	40	5.604	-10.275	10.336	1.00	54.79
ATOM	294	CG1	VAL	40	6.752	-9.471	10.927	1.00	55.17

FIG.11A-7

ATOM	295	CG2	VAL	40	4.453	-9.352	9.963	1.00	49.52
ATOM	296	C	VAL	40	4.995	-12.016	8.656	1.00	55.18
ATOM	297	O	VAL	40	3.925	-11.608	8.206	1.00	54.97
ATOM	298	N	ASP	41	5.277	-13.307	8.801	1.00	57.61
ATOM	299	CA	ASP	41	4.327	-14.352	8.437	1.00	59.72
ATOM	300	CB	ASP	41	5.077	-15.653	8.142	1.00	63.63
ATOM	301	CG	ASP	41	4.183	-16.719	7.545	1.00	70.52
ATOM	302	OD1	ASP	41	3.141	-17.036	8.157	1.00	69.83
ATOM	303	OD2	ASP	41	4.525	-17.244	6.465	1.00	74.90
ATOM	304	C	ASP	41	3.352	-14.561	9.595	1.00	58.84
ATOM	305	O	ASP	41	3.675	-15.233	10.575	1.00	57.65
ATOM	306	N	MET	42	2.159	-13.984	9.477	1.00	59.02
ATOM	307	CA	MET	42	1.142	-14.092	10.520	1.00	60.04
ATOM	308	CB	MET	42	-0.155	-13.415	10.064	1.00	59.22
ATOM	309	CG	MET	42	-0.036	-11.910	9.863	1.00	60.26
ATOM	310	SD	MET	42	-1.552	-11.157	9.227	1.00	69.49
ATOM	311	CE	MET	42	-2.295	-10.547	10.725	1.00	66.84
ATOM	312	C	MET	42	0.847	-15.532	10.931	1.00	60.57
ATOM	313	O	MET	42	0.297	-15.774	12.006	1.00	60.43
ATOM	314	N	ALA	43	1.216	-16.483	10.078	1.00	61.75
ATOM	315	CA	ALA	43	0.983	-17.898	10.358	1.00	63.27
ATOM	316	CB	ALA	43	0.675	-18.642	9.061	1.00	64.51
ATOM	317	C	ALA	43	2.180	-18.538	11.054	1.00	63.20
ATOM	318	O	ALA	43	2.055	-19.596	11.672	1.00	64.09
ATOM	319	N	ALA	44	3.337	-17.894	10.950	1.00	62.86
ATOM	320	CA	ALA	44	4.555	-18.404	11.568	1.00	65.57
ATOM	321	CB	ALA	44	5.777	-17.767	10.910	1.00	67.13
ATOM	322	C	ALA	44	4.566	-18.135	13.071	1.00	69.55
ATOM	323	O	ALA	44	5.527	-17.497	13.550	1.00	69.48
ATOM	324	OT	ALA	44	3.614	-18.571	13.752	1.00	73.84
ATOM	325	CB	CYS	48	1.032	-12.998	16.789	1.00	61.49
ATOM	326	SG	CYS	48	-0.413	-12.709	17.840	1.00	66.53
ATOM	327	C	CYS	48	-0.172	-12.208	14.752	1.00	58.42
ATOM	328	O	CYS	48	0.282	-11.074	14.587	1.00	58.49
ATOM	329	N	CYS	48	1.950	-13.489	14.540	1.00	59.82
ATOM	330	CA	CYS	48	0.697	-13.320	15.332	1.00	59.76
ATOM	331	N	PRO	49	-1.437	-12.524	14.431	1.00	57.61
ATOM	332	CD	PRO	49	-2.015	-13.880	14.439	1.00	59.35
ATOM	333	CA	PRO	49	-2.389	-11.562	13.865	1.00	57.53
ATOM	334	CB	PRO	49	-3.655	-12.397	13.690	1.00	58.94
ATOM	335	CG	PRO	49	-3.112	-13.762	13.407	1.00	60.96
ATOM	336	C	PRO	49	-2.625	-10.340	14.749	1.00	56.62

FIG.11A-8

ATOM	337	O	PRO	49	-2.602	-9.205	14.273	1.00	56.98
ATOM	338	N	GLU	50	-2.856	-10.580	16.036	1.00	55.89
ATOM	339	CA	GLU	50	-3.104	-9.502	16.985	1.00	54.74
ATOM	340	CB	GLU	50	-3.627	-10.072	18.306	1.00	57.44
ATOM	341	CG	GLU	50	-3.950	-9.012	19.348	1.00	66.02
ATOM	342	CD	GLU	50	-4.288	-9.606	20.701	1.00	72.56
ATOM	343	OE1	GLU	50	-3.412	-10.271	21.295	1.00	71.89
ATOM	344	OE2	GLU	50	-5.428	-9.410	21.171	1.00	78.20
ATOM	345	C	GLU	50	-1.846	-8.680	17.256	1.00	51.37
ATOM	346	O	GLU	50	-1.846	-7.458	17.100	1.00	51.31
ATOM	347	N	ALA	51	-0.779	-9.359	17.666	1.00	48.02
ATOM	348	CA	ALA	51	0.487	-8.701	17.969	1.00	45.05
ATOM	349	CB	ALA	51	1.577	-9.747	18.180	1.00	42.33
ATOM	350	C	ALA	51	0.895	-7.734	16.862	1.00	44.76
ATOM	351	O	ALA	51	1.156	-6.558	17.116	1.00	43.03
ATOM	352	N	ILE	52	0.940	-8.234	15.633	1.00	44.08
ATOM	353	CA	ILE	52	1.318	-7.409	14.494	1.00	42.87
ATOM	354	CB	ILE	52	1.402	-8.275	13.199	1.00	43.74
ATOM	355	CG2	ILE	52	0.009	-8.542	12.651	1.00	45.02
ATOM	356	CG1	ILE	52	2.287	-7.588	12.154	1.00	46.00
ATOM	357	CD1	ILE	52	1.728	-6.309	11.590	1.00	46.21
ATOM	358	C	ILE	52	0.309	-6.267	14.321	1.00	39.96
ATOM	359	O	ILE	52	0.686	-5.137	14.006	1.00	38.32
ATOM	360	N	LYS	53	-0.968	-6.560	14.544	1.00	38.61
ATOM	361	CA	LYS	53	-2.012	-5.548	14.412	1.00	38.67
ATOM	362	CB	LYS	53	-3.394	-6.176	14.612	1.00	40.27
ATOM	363	CG	LYS	53	-4.205	-6.289	13.327	1.00	50.21
ATOM	364	CD	LYS	53	-3.501	-7.151	12.289	1.00	54.17
ATOM	365	CE	LYS	53	-4.213	-7.088	10.948	1.00	59.51
ATOM	366	NZ	LYS	53	-4.230	-5.702	10.405	1.00	57.13
ATOM	367	C	LYS	53	-1.829	-4.396	15.396	1.00	37.31
ATOM	368	O	LYS	53	-2.105	-3.240	15.072	1.00	37.14
ATOM	369	N	LYS	54	-1.370	-4.712	16.602	1.00	35.35
ATOM	370	CA	LYS	54	-1.155	-3.685	17.612	1.00	32.72
ATOM	371	CB	LYS	54	-0.959	-4.332	18.984	1.00	32.05
ATOM	372	CG	LYS	54	-0.850	-3.344	20.138	1.00	29.96
ATOM	373	CD	LYS	54	-0.733	-4.081	21.465	1.00	31.32
ATOM	374	CE	LYS	54	-0.720	-3.119	22.644	1.00	32.19
ATOM	375	NZ	LYS	54	-0.527	-3.833	23.939	1.00	32.80
ATOM	376	C	LYS	54	0.070	-2.852	17.240	1.00	30.86
ATOM	377	O	LYS	54	0.086	-1.636	17.432	1.00	29.26
ATOM	378	N	GLU	55	1.092	-3.514	16.703	1.00	30.10

FIG.11A-9

ATOM	379	CA	GLU	55	2.315	-2.832	16.299	1.00	30.95
ATOM	380	CB	GLU	55	3.356	-3.838	15.791	1.00	28.04
ATOM	381	CG	GLU	55	4.719	-3.209	15.511	1.00	29.66
ATOM	382	CD	GLU	55	5.780	-4.224	15.120	1.00	30.54
ATOM	383	OE1	GLU	55	5.708	-5.375	15.595	1.00	32.37
ATOM	384	OE2	GLU	55	6.699	-3.865	14.350	1.00	30.60
ATOM	385	C	GLU	55	2.004	-1.818	15.203	1.00	31.62
ATOM	386	O	GLU	55	2.552	-0.717	15.186	1.00	29.23
ATOM	387	N	ILE	56	1.121	-2.197	14.285	1.00	32.35
ATOM	388	CA	ILE	56	0.741	-1.300	13.203	1.00	31.04
ATOM	389	CB	ILE	56	-0.135	-2.018	12.151	1.00	30.54
ATOM	390	CG2	ILE	56	-0.659	-1.014	11.138	1.00	28.78
ATOM	391	CG1	ILE	56	0.678	-3.108	11.454	1.00	27.54
ATOM	392	CD1	ILE	56	-0.104	-3.863	10.397	1.00	28.92
ATOM	393	C	ILE	56	-0.047	-0.134	13.785	1.00	29.35
ATOM	394	O	ILE	56	0.185	1.022	13.432	1.00	26.97
ATOM	395	N	CYS	57	-0.974	-0.443	14.686	1.00	28.75
ATOM	396	CA	CYS	57	-1.794	0.587	15.314	1.00	30.06
ATOM	397	CB	CYS	57	-2.728	-0.030	16.359	1.00	32.53
ATOM	398	SG	CYS	57	-3.764	1.186	17.224	1.00	42.92
ATOM	399	C	CYS	57	-0.907	1.630	15.986	1.00	27.01
ATOM	400	O	CYS	57	-1.043	2.825	15.742	1.00	27.89
ATOM	401	N	ILE	58	-0.001	1.166	16.838	1.00	23.73
ATOM	402	CA	ILE	58	0.896	2.076	17.538	1.00	24.79
ATOM	403	CB	ILE	58	1.810	1.305	18.522	1.00	29.75
ATOM	404	CG2	ILE	58	2.934	2.212	19.039	1.00	23.87
ATOM	405	CG1	ILE	58	0.968	0.787	19.691	1.00	28.05
ATOM	406	CD1	ILE	58	1.773	0.086	20.780	1.00	29.21
ATOM	407	C	ILE	58	1.735	2.871	16.545	1.00	23.36
ATOM	408	O	ILE	58	1.910	4.077	16.703	1.00	23.90
ATOM	409	N	ASN	59	2.237	2.204	15.509	1.00	23.80
ATOM	410	CA	ASN	59	3.046	2.882	14.498	1.00	25.17
ATOM	411	CB	ASN	59	3.547	1.873	13.461	1.00	28.55
ATOM	412	CG	ASN	59	4.951	1.372	13.764	1.00	31.94
ATOM	413	OD1	ASN	59	5.929	2.102	13.598	1.00	32.03
ATOM	414	ND2	ASN	59	5.055	0.129	14.218	1.00	27.23
ATOM	415	C	ASN	59	2.302	4.023	13.801	1.00	26.97
ATOM	416	O	ASN	59	2.900	5.045	13.457	1.00	24.75
ATOM	417	N	LYS	60	0.999	3.856	13.595	1.00	28.98
ATOM	418	CA	LYS	60	0.207	4.892	12.936	1.00	30.49
ATOM	419	CB	LYS	60	-1.205	4.376	12.635	1.00	33.22
ATOM	420	CG	LYS	60	-1.254	3.289	11.574	1.00	39.31

FIG.11A-10

ATOM	421	CD	LYS	60	-2.689	2.881	11.275	1.00	50.07
ATOM	422	CE	LYS	60	-2.751	1.811	10.199	1.00	63.36
ATOM	423	NZ	LYS	60	-4.156	1.431	9.879	1.00	70.80
ATOM	424	C	LYS	60	0.112	6.167	13.769	1.00	30.79
ATOM	425	O	LYS	60	-0.255	7.225	13.261	1.00	32.02
ATOM	426	N	MET	61	0.453	6.067	15.049	1.00	29.22
ATOM	427	CA	MET	61	0.402	7.214	15.948	1.00	28.15
ATOM	428	CB	MET	61	0.133	6.752	17.383	1.00	26.84
ATOM	429	CG	MET	61	-1.123	5.934	17.601	1.00	33.92
ATOM	430	SD	MET	61	-1.086	5.213	19.267	1.00	36.19
ATOM	431	CE	MET	61	-1.338	6.689	20.282	1.00	35.78
ATOM	432	C	MET	61	1.719	7.982	15.969	1.00	27.73
ATOM	433	O	MET	61	1.773	9.126	16.419	1.00	30.14
ATOM	434	N	LEU	62	2.772	7.346	15.474	1.00	26.12
ATOM	435	CA	LEU	62	4.112	7.921	15.516	1.00	25.23
ATOM	436	CB	LEU	62	5.129	6.786	15.574	1.00	24.11
ATOM	437	CG	LEU	62	4.747	5.617	16.481	1.00	22.84
ATOM	438	CD1	LEU	62	5.836	4.560	16.419	1.00	23.66
ATOM	439	CD2	LEU	62	4.531	6.119	17.905	1.00	26.09
ATOM	440	C	LEU	62	4.546	8.901	14.438	1.00	26.40
ATOM	441	O	LEU	62	4.434	8.629	13.244	1.00	27.81
ATOM	442	N	ASN	63	5.060	10.044	14.883	1.00	25.22
ATOM	443	CA	ASN	63	5.576	11.064	13.981	1.00	24.06
ATOM	444	CB	ASN	63	4.438	11.900	13.388	1.00	28.33
ATOM	445	CG	ASN	63	4.938	12.925	12.399	1.00	31.22
ATOM	446	OD1	ASN	63	5.933	12.696	11.711	1.00	34.87
ATOM	447	ND2	ASN	63	4.249	14.058	12.310	1.00	31.84
ATOM	448	C	ASN	63	6.564	11.961	14.716	1.00	21.00
ATOM	449	O	ASN	63	6.202	13.010	15.240	1.00	20.80
ATOM	450	N	HIS	64	7.818	11.525	14.759	1.00	20.38
ATOM	451	CA	HIS	64	8.869	12.279	15.433	1.00	20.84
ATOM	452	CB	HIS	64	8.896	11.911	16.923	1.00	20.13
ATOM	453	CG	HIS	64	9.818	12.764	17.733	1.00	18.13
ATOM	454	CD2	HIS	64	9.601	13.929	18.387	1.00	15.83
ATOM	455	ND1	HIS	64	11.158	12.479	17.888	1.00	15.42
ATOM	456	CE1	HIS	64	11.726	13.433	18.602	1.00	16.82
ATOM	457	NE2	HIS	64	10.804	14.324	18.917	1.00	17.85
ATOM	458	C	HIS	64	10.221	11.983	14.786	1.00	19.49
ATOM	459	O	HIS	64	10.475	10.863	14.351	1.00	19.75
ATOM	460	N	GLU	65	11.094	12.985	14.733	1.00	21.02
ATOM	461	CA	GLU	65	12.397	12.816	14.100	1.00	21.68
ATOM	462	CB	GLU	65	13.124	14.163	14.000	1.00	24.01

FIG.11A-11

ATOM	463	CG	GLU	65	13.445	14.843	15.322	1.00	33.53
ATOM	464	CD	GLU	65	12.284	15.643	15.885	1.00	41.84
ATOM	465	OE1	GLU	65	12.503	16.371	16.878	1.00	47.89
ATOM	466	OE2	GLU	65	11.158	15.548	15.346	1.00	41.02
ATOM	467	C	GLU	65	13.323	11.781	14.733	1.00	22.44
ATOM	468	O	GLU	65	14.288	11.347	14.100	1.00	21.52
ATOM	469	N	ASN	66	13.038	11.380	15.972	1.00	21.25
ATOM	470	CA	ASN	66	13.873	10.383	16.636	1.00	20.43
ATOM	471	CB	ASN	66	14.389	10.926	17.970	1.00	18.34
ATOM	472	CG	ASN	66	15.360	12.089	17.790	1.00	18.97
ATOM	473	OD1	ASN	66	15.096	13.205	18.234	1.00	19.31
ATOM	474	ND2	ASN	66	16.487	11.827	17.137	1.00	19.95
ATOM	475	C	ASN	66	13.136	9.055	16.841	1.00	20.35
ATOM	476	O	ASN	66	13.463	8.278	17.739	1.00	18.70
ATOM	477	N	VAL	67	12.146	8.807	15.983	1.00	19.53
ATOM	478	CA	VAL	67	11.356	7.582	16.010	1.00	20.23
ATOM	479	CB	VAL	67	9.935	7.840	16.586	1.00	19.48
ATOM	480	CG1	VAL	67	9.074	6.589	16.470	1.00	17.62
ATOM	481	CG2	VAL	67	10.037	8.274	18.046	1.00	19.56
ATOM	482	C	VAL	67	11.231	7.090	14.566	1.00	20.28
ATOM	483	O	VAL	67	10.872	7.862	13.680	1.00	18.26
ATOM	484	N	VAL	68	11.541	5.818	14.333	1.00	19.74
ATOM	485	CA	VAL	68	11.449	5.247	12.991	1.00	20.39
ATOM	486	CB	VAL	68	11.694	3.710	13.015	1.00	18.90
ATOM	487	CG1	VAL	68	11.334	3.093	11.665	1.00	18.65
ATOM	488	CG2	VAL	68	13.155	3.420	13.327	1.00	16.32
ATOM	489	C	VAL	68	10.074	5.542	12.393	1.00	22.68
ATOM	490	O	VAL	68	9.046	5.217	12.986	1.00	22.91
ATOM	491	N	LYS	69	10.068	6.172	11.221	1.00	24.55
ATOM	492	CA	LYS	69	8.833	6.528	10.530	1.00	26.28
ATOM	493	CB	LYS	69	9.129	7.465	9.353	1.00	31.62
ATOM	494	CG	LYS	69	8.623	8.889	9.512	1.00	44.19
ATOM	495	CD	LYS	69	9.589	9.741	10.314	1.00	51.62
ATOM	496	CE	LYS	69	9.187	11.207	10.281	1.00	51.35
ATOM	497	NZ	LYS	69	10.241	12.081	10.865	1.00	48.96
ATOM	498	C	LYS	69	8.103	5.310	9.990	1.00	24.58
ATOM	499	O	LYS	69	8.729	4.348	9.539	1.00	25.04
ATOM	500	N	PHE	70	6.776	5.368	10.040	1.00	25.47
ATOM	501	CA	PHE	70	5.915	4.307	9.527	1.00	26.89
ATOM	502	CB	PHE	70	4.824	3.961	10.545	1.00	29.09
ATOM	503	CG	PHE	70	3.841	2.928	10.060	1.00	27.43
ATOM	504	CD1	PHE	70	4.248	1.621	9.808	1.00	28.02

FIG.11A-12

ATOM	505	CD2	PHE	70	2.504	3.263	9.865	1.00	30.32
ATOM	506	CE1	PHE	70	3.337	0.659	9.372	1.00	31.52
ATOM	507	CE2	PHE	70	1.583	2.310	9.429	1.00	29.79
ATOM	508	CZ	PHE	70	1.999	1.006	9.182	1.00	30.08
ATOM	509	C	PHE	70	5.271	4.874	8.263	1.00	28.21
ATOM	510	O	PHE	70	4.564	5.880	8.318	1.00	28.68
ATOM	511	N	TYR	71	5.522	4.240	7.124	1.00	29.81
ATOM	512	CA	TYR	71	4.959	4.718	5.870	1.00	31.13
ATOM	513	CB	TYR	71	5.954	4.500	4.732	1.00	24.91
ATOM	514	CG	TYR	71	7.285	5.182	4.927	1.00	25.81
ATOM	515	CD1	TYR	71	7.369	6.566	5.078	1.00	28.78
ATOM	516	CE1	TYR	71	8.604	7.199	5.220	1.00	27.30
ATOM	517	CD2	TYR	71	8.465	4.449	4.926	1.00	26.54
ATOM	518	CE2	TYR	71	9.699	5.069	5.065	1.00	24.23
ATOM	519	CZ	TYR	71	9.763	6.442	5.209	1.00	23.46
ATOM	520	OH	TYR	71	10.991	7.056	5.330	1.00	29.32
ATOM	521	C	TYR	71	3.634	4.049	5.520	1.00	34.42
ATOM	522	O	TYR	71	2.842	4.596	4.753	1.00	36.42
ATOM	523	N	GLY	72	3.397	2.865	6.076	1.00	34.34
ATOM	524	CA	GLY	72	2.163	2.149	5.801	1.00	33.61
ATOM	525	C	GLY	72	2.392	0.653	5.757	1.00	34.42
ATOM	526	O	GLY	72	3.511	0.191	5.972	1.00	34.69
ATOM	527	N	HIS	73	1.341	-0.111	5.475	1.00	37.74
ATOM	528	CA	HIS	73	1.463	-1.564	5.413	1.00	40.55
ATOM	529	CB	HIS	73	1.102	-2.174	6.769	1.00	39.94
ATOM	530	CG	HIS	73	-0.340	-2.012	7.141	1.00	41.03
ATOM	531	CD2	HIS	73	-1.017	-0.953	7.642	1.00	38.25
ATOM	532	ND1	HIS	73	-1.265	-3.021	6.986	1.00	42.56
ATOM	533	CE1	HIS	73	-2.452	-2.591	7.377	1.00	39.22
ATOM	534	NE2	HIS	73	-2.329	-1.338	7.779	1.00	37.48
ATOM	535	C	HIS	73	0.576	-2.164	4.325	1.00	42.07
ATOM	536	O	HIS	73	-0.407	-1.553	3.907	1.00	40.35
ATOM	537	N	ARG	74	0.933	-3.363	3.875	1.00	45.26
ATOM	538	CA	ARG	74	0.176	-4.056	2.837	1.00	50.38
ATOM	539	CB	ARG	74	1.022	-4.169	1.567	1.00	55.88
ATOM	540	CG	ARG	74	1.382	-2.819	0.963	1.00	63.87
ATOM	541	CD	ARG	74	2.373	-2.946	-0.184	1.00	70.66
ATOM	542	NE	ARG	74	1.861	-3.752	-1.288	1.00	72.42
ATOM	543	CZ	ARG	74	2.485	-3.897	-2.453	1.00	73.76
ATOM	544	NH1	ARG	74	3.645	-3.289	-2.667	1.00	64.85
ATOM	545	NH2	ARG	74	1.951	-4.650	-3.406	1.00	78.24
ATOM	546	C	ARG	74	-0.262	-5.444	3.302	1.00	52.53

FIG.11A-13

ATOM	547	O	ARG	74	0.550	-6.237	3.785	1.00	50.95
ATOM	548	N	ARG	75	-1.554	-5.725	3.148	1.00	56.77
ATOM	549	CA	ARG	75	-2.138	-7.002	3.550	1.00	61.66
ATOM	550	CB	ARG	75	-3.617	-7.046	3.150	1.00	66.26
ATOM	551	CG	ARG	75	-4.406	-5.800	3.536	1.00	70.07
ATOM	552	CD	ARG	75	-4.471	-5.610	5.043	1.00	75.18
ATOM	553	NE	ARG	75	-5.229	-6.674	5.697	1.00	79.27
ATOM	554	CZ	ARG	75	-5.442	-6.742	7.007	1.00	81.70
ATOM	555	NH1	ARG	75	-4.953	-5.806	7.810	1.00	80.67
ATOM	556	NH2	ARG	75	-6.147	-7.744	7.514	1.00	80.01
ATOM	557	C	ARG	75	-1.404	-8.183	2.917	1.00	62.81
ATOM	558	O	ARG	75	-0.570	-8.821	3.557	1.00	62.78
ATOM	559	N	GLU	76	-1.730	-8.470	1.661	1.00	62.55
ATOM	560	CA	GLU	76	-1.109	-9.565	0.920	1.00	62.56
ATOM	561	CB	GLU	76	0.399	-9.332	0.799	1.00	62.91
ATOM	562	CG	GLU	76	1.081	-10.208	-0.240	1.00	67.69
ATOM	563	CD	GLU	76	0.711	-9.820	-1.659	1.00	71.31
ATOM	564	OE1	GLU	76	1.016	-8.676	-2.058	1.00	70.71
ATOM	565	OE2	GLU	76	0.116	-10.653	-2.374	1.00	73.78
ATOM	566	C	GLU	76	-1.361	-10.931	1.561	1.00	62.35
ATOM	567	O	GLU	76	-0.420	-11.663	1.874	1.00	62.16
ATOM	568	N	GLY	77	-2.632	-11.270	1.751	1.00	61.81
ATOM	569	CA	GLY	77	-2.978	-12.551	2.343	1.00	60.86
ATOM	570	C	GLY	77	-2.625	-12.690	3.814	1.00	60.50
ATOM	571	O	GLY	77	-3.260	-12.078	4.673	1.00	60.41
ATOM	572	N	ASN	78	-1.612	-13.501	4.103	1.00	59.52
ATOM	573	CA	ASN	78	-1.174	-13.732	5.477	1.00	59.24
ATOM	574	CB	ASN	78	-1.096	-15.236	5.756	1.00	62.54
ATOM	575	CG	ASN	78	-2.448	-15.914	5.672	1.00	69.02
ATOM	576	OD1	ASN	78	-3.145	-15.815	4.661	1.00	71.32
ATOM	577	ND2	ASN	78	-2.826	-16.613	6.736	1.00	72.20
ATOM	578	C	ASN	78	0.182	-13.096	5.770	1.00	57.34
ATOM	579	O	ASN	78	0.632	-13.079	6.916	1.00	56.95
ATOM	580	N	ILE	79	0.831	-12.579	4.732	1.00	55.93
ATOM	581	CA	ILE	79	2.136	-11.947	4.889	1.00	54.66
ATOM	582	CB	ILE	79	3.065	-12.281	3.700	1.00	54.22
ATOM	583	CG2	ILE	79	4.399	-11.570	3.864	1.00	53.56
ATOM	584	CG1	ILE	79	3.273	-13.795	3.607	1.00	52.83
ATOM	585	CD1	ILE	79	3.890	-14.415	4.846	1.00	50.48
ATOM	586	C	ILE	79	2.005	-10.433	4.991	1.00	52.67
ATOM	587	O	ILE	79	1.668	-9.767	4.012	1.00	50.87
ATOM	588	N	GLN	80	2.272	-9.895	6.180	1.00	50.66

FIG.11A-14

ATOM	589	CA	GLN	80	2.191	-8.455	6.408	1.00	48.22
ATOM	590	CB	GLN	80	1.944	-8.158	7.891	1.00	50.12
ATOM	591	CG	GLN	80	0.521	-8.399	8.362	1.00	48.27
ATOM	592	CD	GLN	80	-0.494	-7.572	7.594	1.00	49.09
ATOM	593	OE1	GLN	80	-0.372	-6.351	7.493	1.00	45.08
ATOM	594	NE2	GLN	80	-1.506	-8.237	7.049	1.00	58.25
ATOM	595	C	GLN	80	3.469	-7.750	5.966	1.00	46.07
ATOM	596	O	GLN	80	4.572	-8.222	6.238	1.00	45.36
ATOM	597	N	TYR	81	3.307	-6.618	5.288	1.00	45.11
ATOM	598	CA	TYR	81	4.436	-5.829	4.805	1.00	43.61
ATOM	599	CB	TYR	81	4.385	-5.706	3.280	1.00	42.41
ATOM	600	CG	TYR	81	4.641	-7.001	2.545	1.00	43.09
ATOM	601	CD1	TYR	81	5.918	-7.559	2.504	1.00	40.63
ATOM	602	CE1	TYR	81	6.157	-8.756	1.834	1.00	45.03
ATOM	603	CD2	TYR	81	3.606	-7.672	1.896	1.00	41.43
ATOM	604	CE2	TYR	81	3.835	-8.870	1.225	1.00	44.97
ATOM	605	CZ	TYR	81	5.111	-9.405	1.197	1.00	46.87
ATOM	606	OH	TYR	81	5.339	-10.589	0.534	1.00	49.59
ATOM	607	C	TYR	81	4.409	-4.433	5.419	1.00	42.40
ATOM	608	O	TYR	81	3.585	-3.602	5.042	1.00	43.43
ATOM	609	N	LEU	82	5.309	-4.178	6.365	1.00	39.70
ATOM	610	CA	LEU	82	5.372	-2.874	7.010	1.00	37.19
ATOM	611	CB	LEU	82	5.616	-3.028	8.517	1.00	39.36
ATOM	612	CG	LEU	82	4.579	-3.785	9.358	1.00	38.76
ATOM	613	CD1	LEU	82	4.968	-3.697	10.827	1.00	32.68
ATOM	614	CD2	LEU	82	3.199	-3.191	9.155	1.00	39.92
ATOM	615	C	LEU	82	6.485	-2.030	6.397	1.00	34.17
ATOM	616	O	LEU	82	7.659	-2.406	6.445	1.00	32.38
ATOM	617	N	PHE	83	6.112	-0.892	5.820	1.00	33.55
ATOM	618	CA	PHE	83	7.083	0.008	5.209	1.00	31.38
ATOM	619	CB	PHE	83	6.464	0.728	4.011	1.00	36.90
ATOM	620	CG	PHE	83	6.209	-0.173	2.833	1.00	40.96
ATOM	621	CD1	PHE	83	5.310	-1.231	2.930	1.00	42.10
ATOM	622	CD2	PHE	83	6.885	0.024	1.633	1.00	41.38
ATOM	623	CE1	PHE	83	5.088	-2.084	1.848	1.00	41.93
ATOM	624	CE2	PHE	83	6.671	-0.823	0.543	1.00	40.00
ATOM	625	CZ	PHE	83	5.770	-1.879	0.652	1.00	39.51
ATOM	626	C	PHE	83	7.552	1.012	6.251	1.00	28.18
ATOM	627	O	PHE	83	6.797	1.892	6.676	1.00	24.97
ATOM	628	N	LEU	84	8.810	0.869	6.647	1.00	27.73
ATOM	629	CA	LEU	84	9.408	1.715	7.670	1.00	27.95
ATOM	630	CB	LEU	84	9.837	0.837	8.846	1.00	28.57

FIG.11-A15

ATOM	631	CG	LEU	84	8.720	-0.038	9.430	1.00	24.56
ATOM	632	CD1	LEU	84	9.313	-1.254	10.122	1.00	21.64
ATOM	633	CD2	LEU	84	7.874	0.787	10.386	1.00	24.46
ATOM	634	C	LEU	84	10.604	2.508	7.164	1.00	28.88
ATOM	635	O	LEU	84	11.204	2.184	6.138	1.00	28.67
ATOM	636	N	GLU	85	10.949	3.551	7.908	1.00	28.76
ATOM	637	CA	GLU	85	12.072	4.404	7.564	1.00	28.20
ATOM	638	CB	GLU	85	12.170	5.544	8.579	1.00	29.51
ATOM	639	CG	GLU	85	13.371	6.450	8.406	1.00	34.24
ATOM	640	CD	GLU	85	13.405	7.556	9.443	1.00	36.83
ATOM	641	OE1	GLU	85	14.354	8.367	9.418	1.00	36.87
ATOM	642	OE2	GLU	85	12.478	7.613	10.280	1.00	30.28
ATOM	643	C	GLU	85	13.367	3.599	7.551	1.00	27.67
ATOM	644	O	GLU	85	13.645	2.832	8.475	1.00	28.74
ATOM	645	N	TYR	86	14.150	3.760	6.492	1.00	24.64
ATOM	646	CA	TYR	86	15.421	3.059	6.378	1.00	23.98
ATOM	647	CB	TYR	86	15.793	2.870	4.901	1.00	24.65
ATOM	648	CG	TYR	86	17.208	2.376	4.671	1.00	25.72
ATOM	649	CD1	TYR	86	17.652	1.177	5.229	1.00	22.83
ATOM	650	CE1	TYR	86	18.954	0.719	5.014	1.00	20.99
ATOM	651	CD2	TYR	86	18.103	3.108	3.888	1.00	24.91
ATOM	652	CE2	TYR	86	19.404	2.659	3.668	1.00	25.43
ATOM	653	CZ	TYR	86	19.822	1.466	4.234	1.00	24.00
ATOM	654	OH	TYR	86	21.110	1.021	4.030	1.00	31.37
ATOM	655	C	TYR	86	16.499	3.879	7.081	1.00	24.51
ATOM	656	O	TYR	86	16.644	5.075	6.828	1.00	25.53
ATOM	657	N	CYS	87	17.241	3.236	7.974	1.00	23.81
ATOM	658	CA	CYS	87	18.303	3.914	8.714	1.00	24.33
ATOM	659	CB	CYS	87	18.059	3.747	10.218	1.00	21.77
ATOM	660	SG	CYS	87	16.439	4.374	10.742	1.00	22.54
ATOM	661	C	CYS	87	19.637	3.310	8.287	1.00	22.59
ATOM	662	O	CYS	87	20.090	2.310	8.840	1.00	22.98
ATOM	663	N	SER	88	20.263	3.935	7.291	1.00	22.63
ATOM	664	CA	SER	88	21.519	3.452	6.729	1.00	23.13
ATOM	665	CB	SER	88	21.869	4.258	5.470	1.00	23.11
ATOM	666	OG	SER	88	22.008	5.641	5.750	1.00	27.21
ATOM	667	C	SER	88	22.727	3.412	7.656	1.00	24.35
ATOM	668	O	SER	88	23.746	2.808	7.318	1.00	26.40
ATOM	669	N	GLY	89	22.618	4.049	8.818	1.00	23.40
ATOM	670	CA	GLY	89	23.720	4.053	9.764	1.00	21.46
ATOM	671	C	GLY	89	23.777	2.793	10.613	1.00	21.62
ATOM	672	O	GLY	89	24.747	2.566	11.336	1.00	23.85

FIG.11A-16

ATOM	673	N	GLY	90	22.736	1.974	10.523	1.00	19.99
ATOM	674	CA	GLY	90	22.700	0.733	11.275	1.00	19.98
ATOM	675	C	GLY	90	22.263	0.895	12.723	1.00	19.03
ATOM	676	O	GLY	90	21.563	1.845	13.066	1.00	19.39
ATOM	677	N	GLU	91	22.689	-0.036	13.569	1.00	20.36
ATOM	678	CA	GLU	91	22.325	-0.017	14.983	1.00	20.23
ATOM	679	CB	GLU	91	22.202	-1.439	15.522	1.00	21.22
ATOM	680	CG	GLU	91	21.218	-2.329	14.792	1.00	23.61
ATOM	681	CD	GLU	91	21.215	-3.743	15.342	1.00	23.88
ATOM	682	OE1	GLU	91	20.492	-4.594	14.784	1.00	29.99
ATOM	683	OE2	GLU	91	21.934	-4.000	16.334	1.00	22.19
ATOM	684	C	GLU	91	23.334	0.721	15.846	1.00	20.72
ATOM	685	O	GLU	91	24.526	0.739	15.556	1.00	20.19
ATOM	686	N	LEU	92	22.847	1.311	16.932	1.00	19.98
ATOM	687	CA	LEU	92	23.712	2.020	17.864	1.00	19.39
ATOM	688	CB	LEU	92	22.868	2.671	18.963	1.00	18.03
ATOM	689	CG	LEU	92	23.616	3.333	20.122	1.00	19.18
ATOM	690	CD1	LEU	92	24.427	4.513	19.612	1.00	22.62
ATOM	691	CD2	LEU	92	22.596	3.783	21.176	1.00	16.79
ATOM	692	C	LEU	92	24.641	0.989	18.480	1.00	19.97
ATOM	693	O	LEU	92	25.781	1.284	18.834	1.00	19.58
ATOM	694	N	PHE	93	24.134	-0.232	18.599	1.00	20.27
ATOM	695	CA	PHE	93	24.895	-1.322	19.178	1.00	21.88
ATOM	696	CB	PHE	93	24.099	-2.628	19.058	1.00	26.11
ATOM	697	CG	PHE	93	24.813	-3.834	19.611	1.00	28.84
ATOM	698	CD1	PHE	93	25.734	-4.533	18.836	1.00	29.47
ATOM	699	CD2	PHE	93	24.561	-4.274	20.907	1.00	31.53
ATOM	700	CE1	PHE	93	26.393	-5.656	19.344	1.00	30.19
ATOM	701	CE2	PHE	93	25.216	-5.397	21.425	1.00	36.41
ATOM	702	CZ	PHE	93	26.132	-6.088	20.641	1.00	30.51
ATOM	703	C	PHE	93	26.245	-1.458	18.481	1.00	21.58
ATOM	704	O	PHE	93	27.270	-1.675	19.130	1.00	20.32
ATOM	705	N	ASP	94	26.245	-1.300	17.161	1.00	23.68
ATOM	706	CA	ASP	94	27.474	-1.429	16.379	1.00	25.61
ATOM	707	CB	ASP	94	27.118	-1.757	14.925	1.00	30.05
ATOM	708	CG	ASP	94	26.495	-3.138	14.782	1.00	31.43
ATOM	709	OD1	ASP	94	25.725	-3.361	13.827	1.00	33.18
ATOM	710	OD2	ASP	94	26.783	-4.011	15.628	1.00	34.06
ATOM	711	C	ASP	94	28.423	-0.232	16.451	1.00	24.95
ATOM	712	O	ASP	94	29.501	-0.257	15.860	1.00	27.73
ATOM	713	N	ARG	95	28.035	0.801	17.194	1.00	23.99
ATOM	714	CA	ARG	95	28.870	1.991	17.363	1.00	23.16

FIG.11A-17

ATOM	715	CB	ARG	95	28.008	3.255	17.263	1.00	24.65
ATOM	716	CG	ARG	95	27.399	3.479	15.888	1.00	29.91
ATOM	717	CD	ARG	95	28.488	3.806	14.875	1.00	39.68
ATOM	718	NE	ARG	95	29.148	5.055	15.241	1.00	47.46
ATOM	719	CZ	ARG	95	28.687	6.262	14.929	1.00	46.44
ATOM	720	NH1	ARG	95	27.568	6.386	14.227	1.00	39.38
ATOM	721	NH2	ARG	95	29.325	7.346	15.353	1.00	42.03
ATOM	722	C	ARG	95	29.557	1.935	18.727	1.00	22.01
ATOM	723	O	ARG	95	30.340	2.819	19.090	1.00	21.05
ATOM	724	N	ILE	96	29.246	0.885	19.482	1.00	22.78
ATOM	725	CA	ILE	96	29.811	0.680	20.806	1.00	22.43
ATOM	726	CB	ILE	96	28.735	0.146	21.776	1.00	20.79
ATOM	727	CG2	ILE	96	29.332	-0.066	23.160	1.00	20.67
ATOM	728	CG1	ILE	96	27.578	1.146	21.845	1.00	18.29
ATOM	729	CD1	ILE	96	26.357	0.640	22.590	1.00	18.91
ATOM	730	C	ILE	96	30.963	-0.315	20.732	1.00	24.50
ATOM	731	O	ILE	96	30.769	-1.469	20.360	1.00	25.11
ATOM	732	N	GLU	97	32.162	0.136	21.076	1.00	24.39
ATOM	733	CA	GLU	97	33.318	-0.751	21.038	1.00	26.52
ATOM	734	CB	GLU	97	34.605	0.055	20.849	1.00	30.76
ATOM	735	CG	GLU	97	34.830	0.623	19.444	1.00	46.58
ATOM	736	CD	GLU	97	33.846	1.719	19.056	1.00	53.97
ATOM	737	OE1	GLU	97	33.759	2.740	19.776	1.00	50.74
ATOM	738	OE2	GLU	97	33.165	1.561	18.019	1.00	58.08
ATOM	739	C	GLU	97	33.383	-1.570	22.325	1.00	24.68
ATOM	740	O	GLU	97	33.415	-1.020	23.424	1.00	23.06
ATOM	741	N	PRO	98	33.395	-2.906	22.207	1.00	24.21
ATOM	742	CD	PRO	98	33.233	-3.720	20.987	1.00	24.02
ATOM	743	CA	PRO	98	33.454	-3.764	23.392	1.00	23.90
ATOM	744	CB	PRO	98	33.695	-5.147	22.792	1.00	23.15
ATOM	745	CG	PRO	98	32.877	-5.090	21.560	1.00	21.24
ATOM	746	C	PRO	98	34.510	-3.366	24.421	1.00	24.35
ATOM	747	O	PRO	98	35.675	-3.130	24.089	1.00	25.72
ATOM	748	N	ASP	99	34.071	-3.280	25.673	1.00	23.80
ATOM	749	CA	ASP	99	34.919	-2.918	26.797	1.00	25.53
ATOM	750	CB	ASP	99	36.119	-3.870	26.892	1.00	36.73
ATOM	751	CG	ASP	99	35.726	-5.255	27.365	1.00	47.74
ATOM	752	OD1	ASP	99	35.109	-6.005	26.579	1.00	56.16
ATOM	753	OD2	ASP	99	36.030	-5.590	28.531	1.00	54.00
ATOM	754	C	ASP	99	35.430	-1.482	26.826	1.00	24.62
ATOM	755	O	ASP	99	36.168	-1.119	27.741	1.00	26.81
ATOM	756	N	ILE	100	35.066	-0.662	25.841	1.00	23.29

FIG.11-A18

ATOM	757	CA	ILE	100	35.532	0.721	25.862	1.00	23.28
ATOM	758	CB	ILE	100	36.625	1.000	24.786	1.00	28.85
ATOM	759	CG2	ILE	100	37.699	-0.076	24.842	1.00	30.41
ATOM	760	CG1	ILE	100	36.017	1.042	23.393	1.00	37.12
ATOM	761	CD1	ILE	100	37.017	1.438	22.311	1.00	50.18
ATOM	762	C	ILE	100	34.403	1.737	25.699	1.00	20.45
ATOM	763	O	ILE	100	34.413	2.771	26.354	1.00	20.39
ATOM	764	N	GLY	101	33.447	1.445	24.823	1.00	19.63
ATOM	765	CA	GLY	101	32.334	2.355	24.610	1.00	19.62
ATOM	766	C	GLY	101	32.521	3.227	23.384	1.00	18.97
ATOM	767	O	GLY	101	32.745	2.721	22.285	1.00	19.10
ATOM	768	N	MET	102	32.410	4.539	23.570	1.00	18.46
ATOM	769	CA	MET	102	32.583	5.506	22.486	1.00	17.81
ATOM	770	CB	MET	102	31.291	5.655	21.676	1.00	19.03
ATOM	771	CG	MET	102	30.170	6.358	22.449	1.00	19.18
ATOM	772	SD	MET	102	28.677	6.592	21.435	1.00	16.18
ATOM	773	CE	MET	102	28.107	4.874	21.273	1.00	15.36
ATOM	774	C	MET	102	32.931	6.853	23.120	1.00	18.77
ATOM	775	O	MET	102	32.784	7.028	24.331	1.00	19.16
ATOM	776	N	PRO	103	33.403	7.821	22.317	1.00	18.19
ATOM	777	CD	PRO	103	33.736	7.749	20.882	1.00	16.39
ATOM	778	CA	PRO	103	33.749	9.138	22.863	1.00	18.51
ATOM	779	CB	PRO	103	34.109	9.940	21.619	1.00	17.03
ATOM	780	CG	PRO	103	34.696	8.903	20.725	1.00	15.88
ATOM	781	C	PRO	103	32.562	9.741	23.614	1.00	19.83
ATOM	782	O	PRO	103	31.437	9.710	23.126	1.00	19.36
ATOM	783	N	GLU	104	32.823	10.290	24.794	1.00	18.81
ATOM	784	CA	GLU	104	31.771	10.873	25.617	1.00	19.36
ATOM	785	CB	GLU	104	32.386	11.511	26.864	1.00	17.66
ATOM	786	CG	GLU	104	31.406	11.735	27.996	1.00	16.18
ATOM	787	CD	GLU	104	32.058	12.320	29.231	1.00	21.03
ATOM	788	OE1	GLU	104	31.679	13.448	29.619	1.00	21.27
ATOM	789	OE2	GLU	104	32.946	11.657	29.819	1.00	19.74
ATOM	790	C	GLU	104	30.871	11.880	24.898	1.00	19.92
ATOM	791	O	GLU	104	29.653	11.886	25.105	1.00	19.71
ATOM	792	N	PRO	105	31.448	12.748	24.049	1.00	20.08
ATOM	793	CD	PRO	105	32.877	13.000	23.789	1.00	20.80
ATOM	794	CA	PRO	105	30.607	13.723	23.342	1.00	16.33
ATOM	795	CB	PRO	105	31.621	14.529	22.530	1.00	16.90
ATOM	796	CG	PRO	105	32.875	14.459	23.403	1.00	16.88
ATOM	797	C	PRO	105	29.572	13.017	22.452	1.00	16.27
ATOM	798	O	PRO	105	28.424	13.452	22.344	1.00	17.44

FIG.11A-19

ATOM	799	N	ASP	106	29.995	11.934	21.809	1.00	15.51
ATOM	800	CA	ASP	106	29.119	11.153	20.938	1.00	17.98
ATOM	801	CB	ASP	106	29.906	10.029	20.264	1.00	20.63
ATOM	802	CG	ASP	106	30.890	10.530	19.224	1.00	26.04
ATOM	803	OD1	ASP	106	31.277	11.712	19.273	1.00	27.36
ATOM	804	OD2	ASP	106	31.290	9.721	18.364	1.00	31.22
ATOM	805	C	ASP	106	28.001	10.522	21.771	1.00	15.08
ATOM	806	O	ASP	106	26.829	10.515	21.375	1.00	16.13
ATOM	807	N	ALA	107	28.371	9.980	22.925	1.00	14.46
ATOM	808	CA	ALA	107	27.392	9.348	23.802	1.00	16.06
ATOM	809	CB	ALA	107	28.095	8.697	24.989	1.00	14.46
ATOM	810	C	ALA	107	26.363	10.373	24.288	1.00	15.73
ATOM	811	O	ALA	107	25.163	10.077	24.372	1.00	15.16
ATOM	812	N	GLN	108	26.828	11.577	24.603	1.00	14.18
ATOM	813	CA	GLN	108	25.932	12.630	25.075	1.00	14.33
ATOM	814	CB	GLN	108	26.722	13.874	25.492	1.00	17.52
ATOM	815	CG	GLN	108	25.868	14.876	26.277	1.00	16.31
ATOM	816	CD	GLN	108	26.454	16.283	26.303	1.00	18.32
ATOM	817	OE1	GLN	108	26.514	16.924	27.358	1.00	20.27
ATOM	818	NE2	GLN	108	26.859	16.777	25.145	1.00	12.37
ATOM	819	C	GLN	108	24.927	13.029	23.997	1.00	15.75
ATOM	820	O	GLN	108	23.745	13.212	24.286	1.00	14.23
ATOM	821	N	ARG	109	25.402	13.185	22.761	1.00	15.23
ATOM	822	CA	ARG	109	24.526	13.555	21.649	1.00	13.42
ATOM	823	CB	ARG	109	25.356	13.754	20.373	1.00	13.79
ATOM	824	CG	ARG	109	24.552	14.236	19.160	1.00	17.49
ATOM	825	CD	ARG	109	25.408	14.272	17.902	1.00	23.46
ATOM	826	NE	ARG	109	25.536	12.928	17.355	1.00	31.04
ATOM	827	CZ	ARG	109	24.873	12.482	16.294	1.00	23.24
ATOM	828	NH1	ARG	109	24.035	13.274	15.636	1.00	27.75
ATOM	829	NH2	ARG	109	25.034	11.227	15.910	1.00	29.28
ATOM	830	C	ARG	109	23.473	12.458	21.422	1.00	12.94
ATOM	831	O	ARG	109	22.285	12.746	21.243	1.00	14.78
ATOM	832	N	PHE	110	23.904	11.199	21.424	1.00	11.75
ATOM	833	CA	PHE	110	22.963	10.099	21.218	1.00	11.64
ATOM	834	CB	PHE	110	23.681	8.752	21.151	1.00	11.80
ATOM	835	CG	PHE	110	24.421	8.513	19.868	1.00	16.38
ATOM	836	CD1	PHE	110	23.818	8.763	18.633	1.00	18.08
ATOM	837	CD2	PHE	110	25.714	8.003	19.894	1.00	15.97
ATOM	838	CE1	PHE	110	24.502	8.505	17.436	1.00	18.38
ATOM	839	CE2	PHE	110	26.401	7.741	18.713	1.00	16.67
ATOM	840	CZ	PHE	110	25.798	7.991	17.481	1.00	14.35

FIG.11A-20

ATOM	841	C	PHE	110	21.962	10.059	22.366	1.00	12.75
ATOM	842	O	PHE	110	20.777	9.777	22.155	1.00	13.13
ATOM	843	N	PHE	111	22.435	10.339	23.579	1.00	12.26
ATOM	844	CA	PHE	111	21.554	10.325	24.743	1.00	14.38
ATOM	845	CB	PHE	111	22.367	10.450	26.039	1.00	15.94
ATOM	846	CG	PHE	111	21.565	10.174	27.273	1.00	13.02
ATOM	847	CD1	PHE	111	21.146	8.877	27.566	1.00	12.96
ATOM	848	CD2	PHE	111	21.183	11.212	28.119	1.00	9.52
ATOM	849	CE1	PHE	111	20.354	8.617	28.683	1.00	10.93
ATOM	850	CE2	PHE	111	20.391	10.969	29.239	1.00	9.75
ATOM	851	CZ	PHE	111	19.971	9.662	29.523	1.00	9.91
ATOM	852	C	PHE	111	20.519	11.454	24.655	1.00	12.76
ATOM	853	O	PHE	111	19.366	11.278	25.035	1.00	13.45
ATOM	854	N	HIS	112	20.938	12.608	24.144	1.00	13.86
ATOM	855	CA	HIS	112	20.027	13.742	23.970	1.00	14.60
ATOM	856	CB	HIS	112	20.760	14.924	23.331	1.00	15.24
ATOM	857	CG	HIS	112	21.699	15.642	24.249	1.00	15.45
ATOM	858	CD2	HIS	112	21.734	15.739	25.599	1.00	17.90
ATOM	859	ND1	HIS	112	22.718	16.444	23.779	1.00	17.44
ATOM	860	CE1	HIS	112	23.336	17.009	24.802	1.00	15.77
ATOM	861	NE2	HIS	112	22.757	16.598	25.918	1.00	22.23
ATOM	862	C	HIS	112	18.903	13.339	23.019	1.00	15.61
ATOM	863	O	HIS	112	17.726	13.619	23.263	1.00	16.06
ATOM	864	N	GLN	113	19.276	12.699	21.915	1.00	14.44
ATOM	865	CA	GLN	113	18.294	12.283	20.925	1.00	14.83
ATOM	866	CB	GLN	113	18.998	11.869	19.635	1.00	12.67
ATOM	867	CG	GLN	113	19.743	13.047	19.012	1.00	12.96
ATOM	868	CD	GLN	113	20.508	12.662	17.764	1.00	22.01
ATOM	869	OE1	GLN	113	20.468	11.514	17.327	1.00	25.13
ATOM	870	NE2	GLN	113	21.218	13.625	17.186	1.00	21.52
ATOM	871	C	GLN	113	17.406	11.170	21.450	1.00	14.34
ATOM	872	O	GLN	113	16.218	11.124	21.140	1.00	13.52
ATOM	873	N	LEU	114	17.970	10.294	22.273	1.00	14.36
ATOM	874	CA	LEU	114	17.177	9.217	22.863	1.00	13.96
ATOM	875	CB	LEU	114	18.075	8.287	23.683	1.00	13.60
ATOM	876	CG	LEU	114	17.404	7.167	24.485	1.00	14.47
ATOM	877	CD1	LEU	114	16.559	6.292	23.575	1.00	12.86
ATOM	878	CD2	LEU	114	18.491	6.320	25.175	1.00	11.34
ATOM	879	C	LEU	114	16.109	9.848	23.775	1.00	13.12
ATOM	880	O	LEU	114	14.925	9.483	23.730	1.00	12.42
ATOM	881	N	MET	115	16.521	10.806	24.597	1.00	13.13
ATOM	882	CA	MET	115	15.568	11.476	25.486	1.00	14.41

FIG.11A-21

ATOM	883	CB	MET	115	16.274	12.516	26.367	1.00	13.67
ATOM	884	CG	MET	115	17.130	11.938	27.481	1.00	16.47
ATOM	885	SD	MET	115	16.170	10.931	28.639	1.00	16.82
ATOM	886	CE	MET	115	16.565	9.273	27.955	1.00	11.48
ATOM	887	C	MET	115	14.467	12.175	24.685	1.00	14.97
ATOM	888	O	MET	115	13.297	12.136	25.059	1.00	15.73
ATOM	889	N	ALA	116	14.842	12.819	23.585	1.00	16.10
ATOM	890	CA	ALA	116	13.859	13.509	22.752	1.00	15.36
ATOM	891	CB	ALA	116	14.551	14.203	21.581	1.00	14.43
ATOM	892	C	ALA	116	12.818	12.508	22.244	1.00	15.44
ATOM	893	O	ALA	116	11.617	12.785	22.269	1.00	17.74
ATOM	894	N	GLY	117	13.286	11.342	21.815	1.00	13.85
ATOM	895	CA	GLY	117	12.379	10.322	21.312	1.00	13.18
ATOM	896	C	GLY	117	11.490	9.760	22.406	1.00	13.23
ATOM	897	O	GLY	117	10.294	9.563	22.204	1.00	15.51
ATOM	898	N	VAL	118	12.068	9.484	23.571	1.00	13.22
ATOM	899	CA	VAL	118	11.275	8.944	24.669	1.00	13.42
ATOM	900	CB	VAL	118	12.184	8.412	25.790	1.00	12.92
ATOM	901	CG1	VAL	118	11.343	7.955	26.981	1.00	12.41
ATOM	902	CG2	VAL	118	12.999	7.250	25.256	1.00	11.09
ATOM	903	C	VAL	118	10.277	9.964	25.228	1.00	14.91
ATOM	904	O	VAL	118	9.150	9.598	25.581	1.00	15.74
ATOM	905	N	VAL	119	10.677	11.230	25.320	1.00	15.14
ATOM	906	CA	VAL	119	9.764	12.274	25.809	1.00	15.80
ATOM	907	CB	VAL	119	10.428	13.682	25.807	1.00	15.22
ATOM	908	CG1	VAL	119	9.360	14.777	25.915	1.00	16.36
ATOM	909	CG2	VAL	119	11.383	13.805	26.988	1.00	10.99
ATOM	910	C	VAL	119	8.549	12.318	24.889	1.00	15.40
ATOM	911	O	VAL	119	7.401	12.462	25.341	1.00	16.23
ATOM	912	N	TYR	120	8.809	12.196	23.596	1.00	13.60
ATOM	913	CA	TYR	120	7.737	12.226	22.610	1.00	15.80
ATOM	914	CB	TYR	120	8.321	12.168	21.201	1.00	14.64
ATOM	915	CG	TYR	120	7.266	11.942	20.151	1.00	16.47
ATOM	916	CD1	TYR	120	6.407	12.969	19.774	1.00	17.46
ATOM	917	CE1	TYR	120	5.373	12.742	18.861	1.00	16.07
ATOM	918	CD2	TYR	120	7.080	10.685	19.593	1.00	14.78
ATOM	919	CE2	TYR	120	6.055	10.448	18.679	1.00	21.86
ATOM	920	CZ	TYR	120	5.205	11.482	18.321	1.00	23.00
ATOM	921	OH	TYR	120	4.176	11.243	17.433	1.00	24.99
ATOM	922	C	TYR	120	6.774	11.059	22.818	1.00	17.10
ATOM	923	O	TYR	120	5.553	11.247	22.910	1.00	15.76
ATOM	924	N	LEU	121	7.320	9.847	22.880	1.00	14.94

FIG.11A-22

ATOM	925	CA	LEU	121	6.491	8.670	23.074	1.00	14.73
ATOM	926	CB	LEU	121	7.351	7.407	23.136	1.00	14.27
ATOM	927	CG	LEU	121	8.129	7.046	21.867	1.00	15.46
ATOM	928	CD1	LEU	121	8.970	5.796	22.125	1.00	15.26
ATOM	929	CD2	LEU	121	7.165	6.825	20.711	1.00	11.93
ATOM	930	C	LEU	121	5.661	8.782	24.346	1.00	16.08
ATOM	931	O	LEU	121	4.453	8.565	24.328	1.00	14.61
ATOM	932	N	HIS	122	6.309	9.126	25.452	1.00	14.83
ATOM	933	CA	HIS	122	5.594	9.234	26.710	1.00	15.63
ATOM	934	CB	HIS	122	6.585	9.508	27.842	1.00	15.63
ATOM	935	CG	HIS	122	7.434	8.321	28.179	1.00	12.77
ATOM	936	CD2	HIS	122	7.432	7.061	27.686	1.00	12.46
ATOM	937	ND1	HIS	122	8.402	8.349	29.160	1.00	12.14
ATOM	938	CE1	HIS	122	8.957	7.153	29.260	1.00	11.43
ATOM	939	NE2	HIS	122	8.385	6.352	28.377	1.00	12.08
ATOM	940	C	HIS	122	4.515	10.307	26.646	1.00	17.17
ATOM	941	O	HIS	122	3.452	10.163	27.246	1.00	17.14
ATOM	942	N	GLY	123	4.783	11.362	25.886	1.00	17.18
ATOM	943	CA	GLY	123	3.818	12.439	25.755	1.00	19.68
ATOM	944	C	GLY	123	2.536	12.000	25.071	1.00	19.70
ATOM	945	O	GLY	123	1.468	12.559	25.333	1.00	22.02
ATOM	946	N	ILE	124	2.636	11.006	24.195	1.00	18.52
ATOM	947	CA	ILE	124	1.468	10.489	23.485	1.00	20.43
ATOM	948	CB	ILE	124	1.807	10.171	21.992	1.00	26.21
ATOM	949	CG2	ILE	124	2.795	9.024	21.896	1.00	22.32
ATOM	950	CG1	ILE	124	0.531	9.825	21.219	1.00	43.02
ATOM	951	CD1	ILE	124	-0.447	10.975	21.093	1.00	56.77
ATOM	952	C	ILE	124	0.922	9.246	24.200	1.00	19.54
ATOM	953	O	ILE	124	0.023	8.569	23.705	1.00	20.58
ATOM	954	N	GLY	125	1.468	8.953	25.379	1.00	19.44
ATOM	955	CA	GLY	125	0.989	7.816	26.148	1.00	17.08
ATOM	956	C	GLY	125	1.490	6.438	25.753	1.00	15.22
ATOM	957	O	GLY	125	0.872	5.425	26.100	1.00	15.72
ATOM	958	N	ILE	126	2.593	6.368	25.022	1.00	14.59
ATOM	959	CA	ILE	126	3.098	5.054	24.669	1.00	15.92
ATOM	960	CB	ILE	126	3.197	4.831	23.121	1.00	23.85
ATOM	961	CG2	ILE	126	1.985	5.439	22.415	1.00	21.96
ATOM	962	CG1	ILE	126	4.478	5.425	22.565	1.00	25.44
ATOM	963	CD1	ILE	126	4.761	4.944	21.151	1.00	32.08
ATOM	964	C	ILE	126	4.452	4.759	25.304	1.00	14.58
ATOM	965	O	ILE	126	5.301	5.645	25.466	1.00	13.21
ATOM	966	N	THR	127	4.619	3.513	25.725	1.00	15.33

FIG.11A-23

ATOM	967	CA	THR	127	5.884	3.077	26.301	1.00	16.98
ATOM	968	CB	THR	127	5.710	2.492	27.730	1.00	21.08
ATOM	969	OG1	THR	127	6.963	1.951	28.171	1.00	42.01
ATOM	970	CG2	THR	127	4.657	1.398	27.753	1.00	8.51
ATOM	971	C	THR	127	6.458	2.024	25.350	1.00	15.46
ATOM	972	O	THR	127	5.738	1.154	24.862	1.00	13.84
ATOM	973	N	HIS	128	7.757	2.113	25.084	1.00	16.45
ATOM	974	CA	HIS	128	8.415	1.189	24.152	1.00	14.14
ATOM	975	CB	HIS	128	9.736	1.813	23.696	1.00	16.06
ATOM	976	CG	HIS	128	10.479	0.991	22.693	1.00	19.22
ATOM	977	CD2	HIS	128	10.596	1.113	21.349	1.00	20.26
ATOM	978	ND1	HIS	128	11.214	-0.121	23.043	1.00	17.03
ATOM	979	CE1	HIS	128	11.754	-0.647	21.958	1.00	19.24
ATOM	980	NE2	HIS	128	11.394	0.082	20.916	1.00	19.76
ATOM	981	C	HIS	128	8.635	-0.199	24.755	1.00	13.34
ATOM	982	O	HIS	128	8.422	-1.219	24.087	1.00	13.46
ATOM	983	N	ARG	129	9.044	-0.215	26.025	1.00	12.33
ATOM	984	CA	ARG	129	9.283	-1.427	26.820	1.00	13.03
ATOM	985	CB	ARG	129	7.998	-2.267	26.897	1.00	11.47
ATOM	986	CG	ARG	129	6.825	-1.460	27.467	1.00	16.16
ATOM	987	CD	ARG	129	5.740	-2.334	28.093	1.00	15.62
ATOM	988	NE	ARG	129	5.028	-3.116	27.086	1.00	17.92
ATOM	989	CZ	ARG	129	3.963	-3.861	27.354	1.00	19.53
ATOM	990	NH1	ARG	129	3.494	-3.919	28.599	1.00	15.95
ATOM	991	NH2	ARG	129	3.368	-4.544	26.382	1.00	20.39
ATOM	992	C	ARG	129	10.464	-2.327	26.468	1.00	14.38
ATOM	993	O	ARG	129	10.659	-3.371	27.097	1.00	14.82
ATOM	994	N	ASP	130	11.257	-1.939	25.478	1.00	13.77
ATOM	995	CA	ASP	130	12.427	-2.743	25.126	1.00	14.20
ATOM	996	CB	ASP	130	12.055	-3.833	24.111	1.00	14.89
ATOM	997	CG	ASP	130	13.050	-4.990	24.105	1.00	13.64
ATOM	998	OD1	ASP	130	13.026	-5.793	23.144	1.00	16.40
ATOM	999	OD2	ASP	130	13.850	-5.111	25.058	1.00	14.09
ATOM	1000	C	ASP	130	13.548	-1.877	24.561	1.00	12.69
ATOM	1001	O	ASP	130	14.166	-2.222	23.554	1.00	13.46
ATOM	1002	N	ILE	131	13.820	-0.751	25.214	1.00	13.80
ATOM	1003	CA	ILE	131	14.874	0.146	24.748	1.00	14.84
ATOM	1004	CB	ILE	131	14.779	1.517	25.449	1.00	15.30
ATOM	1005	CG2	ILE	131	15.976	2.412	25.055	1.00	13.40
ATOM	1006	CG1	ILE	131	13.458	2.185	25.057	1.00	14.31
ATOM	1007	CD1	ILE	131	13.093	3.399	25.917	1.00	15.14
ATOM	1008	C	ILE	131	16.244	-0.469	25.008	1.00	14.20

FIG.11A-24

ATOM	1009	O	ILE	131	16.543	-0.878	26.115	1.00	14.42
ATOM	1010	N	LYS	132	17.054	-0.544	23.959	1.00	13.66
ATOM	1011	CA	LYS	132	18.405	-1.096	24.020	1.00	12.59
ATOM	1012	CB	LYS	132	18.376	-2.623	24.187	1.00	13.39
ATOM	1013	CG	LYS	132	17.494	-3.375	23.194	1.00	16.12
ATOM	1014	CD	LYS	132	17.518	-4.865	23.500	1.00	15.73
ATOM	1015	CE	LYS	132	16.670	-5.666	22.520	1.00	18.36
ATOM	1016	NZ	LYS	132	16.639	-7.121	22.872	1.00	16.42
ATOM	1017	C	LYS	132	19.084	-0.703	22.715	1.00	13.57
ATOM	1018	O	LYS	132	18.413	-0.351	21.749	1.00	15.48
ATOM	1019	N	PRO	133	20.424	-0.769	22.665	1.00	14.76
ATOM	1020	CD	PRO	133	21.328	-1.231	23.731	1.00	16.68
ATOM	1021	CA	PRO	133	21.188	-0.397	21.467	1.00	15.75
ATOM	1022	CB	PRO	133	22.622	-0.746	21.858	1.00	14.35
ATOM	1023	CG	PRO	133	22.612	-0.538	23.363	1.00	16.22
ATOM	1024	C	PRO	133	20.758	-1.055	20.162	1.00	16.05
ATOM	1025	O	PRO	133	20.868	-0.441	19.096	1.00	18.14
ATOM	1026	N	GLU	134	20.265	-2.289	20.246	1.00	15.05
ATOM	1027	CA	GLU	134	19.820	-3.010	19.061	1.00	17.14
ATOM	1028	CB	GLU	134	19.562	-4.488	19.404	1.00	15.98
ATOM	1029	CG	GLU	134	20.792	-5.246	19.898	1.00	21.80
ATOM	1030	CD	GLU	134	20.945	-5.241	21.415	1.00	24.82
ATOM	1031	OE1	GLU	134	20.669	-4.207	22.067	1.00	18.91
ATOM	1032	OE2	GLU	134	21.363	-6.287	21.957	1.00	27.97
ATOM	1033	C	GLU	134	18.554	-2.389	18.470	1.00	18.34
ATOM	1034	O	GLU	134	18.276	-2.539	17.280	1.00	21.57
ATOM	1035	N	ASN	135	17.785	-1.698	19.307	1.00	18.40
ATOM	1036	CA	ASN	135	16.545	-1.063	18.867	1.00	17.42
ATOM	1037	CB	ASN	135	15.407	-1.373	19.851	1.00	16.38
ATOM	1038	CG	ASN	135	14.881	-2.788	19.697	1.00	21.05
ATOM	1039	OD1	ASN	135	14.895	-3.344	18.596	1.00	25.80
ATOM	1040	ND2	ASN	135	14.397	-3.372	20.791	1.00	18.14
ATOM	1041	C	ASN	135	16.663	0.448	18.687	1.00	17.18
ATOM	1042	O	ASN	135	15.656	1.157	18.628	1.00	18.63
ATOM	1043	N	LEU	136	17.895	0.935	18.609	1.00	15.45
ATOM	1044	CA	LEU	136	18.149	2.356	18.399	1.00	13.88
ATOM	1045	CB	LEU	136	18.902	2.944	19.597	1.00	14.66
ATOM	1046	CG	LEU	136	18.121	2.860	20.919	1.00	13.43
ATOM	1047	CD1	LEU	136	18.987	3.330	22.082	1.00	9.48
ATOM	1048	CD2	LEU	136	16.856	3.724	20.826	1.00	16.23
ATOM	1049	C	LEU	136	18.984	2.416	17.122	1.00	15.09
ATOM	1050	O	LEU	136	20.162	2.068	17.120	1.00	15.49

FIG.11A-25

ATOM	1051	N	LEU	137	18.346	2.824	16.031	1.00	16.71
ATOM	1052	CA	LEU	137	19.002	2.884	14.729	1.00	18.73
ATOM	1053	CB	LEU	137	18.025	2.408	13.650	1.00	18.99
ATOM	1054	CG	LEU	137	17.362	1.067	13.998	1.00	20.11
ATOM	1055	CD1	LEU	137	16.443	0.625	12.863	1.00	21.15
ATOM	1056	CD2	LEU	137	18.438	0.019	14.257	1.00	17.16
ATOM	1057	C	LEU	137	19.532	4.274	14.400	1.00	19.64
ATOM	1058	O	LEU	137	19.152	5.259	15.029	1.00	18.56
ATOM	1059	N	LEU	138	20.416	4.345	13.406	1.00	20.11
ATOM	1060	CA	LEU	138	21.030	5.605	13.012	1.00	21.10
ATOM	1061	CB	LEU	138	22.538	5.569	13.294	1.00	23.33
ATOM	1062	CG	LEU	138	23.028	5.317	14.724	1.00	24.15
ATOM	1063	CD1	LEU	138	22.444	6.368	15.650	1.00	21.36
ATOM	1064	CD2	LEU	138	22.620	3.921	15.169	1.00	27.70
ATOM	1065	C	LEU	138	20.825	5.872	11.526	1.00	23.67
ATOM	1066	O	LEU	138	20.963	4.959	10.707	1.00	23.81
ATOM	1067	N	ASP	139	20.498	7.116	11.184	1.00	24.02
ATOM	1068	CA	ASP	139	20.298	7.481	9.784	1.00	24.89
ATOM	1069	CB	ASP	139	19.295	8.642	9.657	1.00	23.61
ATOM	1070	CG	ASP	139	19.861	9.974	10.120	1.00	24.18
ATOM	1071	OD1	ASP	139	19.136	10.986	10.021	1.00	27.10
ATOM	1072	OD2	ASP	139	21.019	10.020	10.576	1.00	24.71
ATOM	1073	C	ASP	139	21.642	7.857	9.173	1.00	24.93
ATOM	1074	O	ASP	139	22.687	7.630	9.781	1.00	26.58
ATOM	1075	N	GLU	140	21.622	8.426	7.971	1.00	25.87
ATOM	1076	CA	GLU	140	22.857	8.808	7.296	1.00	28.66
ATOM	1077	CB	GLU	140	22.556	9.284	5.866	1.00	30.20
ATOM	1078	CG	GLU	140	21.489	10.364	5.756	1.00	39.13
ATOM	1079	CD	GLU	140	20.119	9.881	6.200	1.00	47.21
ATOM	1080	OE1	GLU	140	19.686	8.808	5.732	1.00	50.57
ATOM	1081	OE2	GLU	140	19.474	10.576	7.013	1.00	52.55
ATOM	1082	C	GLU	140	23.682	9.866	8.032	1.00	28.46
ATOM	1083	O	GLU	140	24.905	9.914	7.882	1.00	29.94
ATOM	1084	N	ARG	141	23.022	10.710	8.821	1.00	27.37
ATOM	1085	CA	ARG	141	23.715	11.756	9.576	1.00	27.01
ATOM	1086	CB	ARG	141	22.942	13.076	9.479	1.00	30.09
ATOM	1087	CG	ARG	141	22.830	13.619	8.059	1.00	37.24
ATOM	1088	CD	ARG	141	22.072	14.941	7.994	1.00	44.03
ATOM	1089	NE	ARG	141	22.712	15.992	8.783	1.00	54.80
ATOM	1090	CZ	ARG	141	22.445	16.242	10.062	1.00	62.47
ATOM	1091	NH1	ARG	141	21.542	15.519	10.711	1.00	60.81
ATOM	1092	NH2	ARG	141	23.084	17.218	10.695	1.00	64.44

FIG.11A-26

ATOM	1093	C	ARG	141	23.891	11.362	11.045	1.00	25.81
ATOM	1094	O	ARG	141	24.141	12.206	11.909	1.00	26.51
ATOM	1095	N	ASP	142	23.779	10.066	11.312	1.00	24.59
ATOM	1096	CA	ASP	142	23.909	9.532	12.664	1.00	25.48
ATOM	1097	CB	ASP	142	25.296	9.822	13.251	1.00	25.98
ATOM	1098	CG	ASP	142	26.350	8.865	12.743	1.00	30.74
ATOM	1099	OD1	ASP	142	26.006	7.694	12.494	1.00	30.35
ATOM	1100	OD2	ASP	142	27.521	9.272	12.608	1.00	40.27
ATOM	1101	C	ASP	142	22.845	10.022	13.634	1.00	22.57
ATOM	1102	O	ASP	142	23.102	10.139	14.834	1.00	22.18
ATOM	1103	N	ASN	143	21.655	10.314	13.125	1.00	22.09
ATOM	1104	CA	ASN	143	20.563	10.733	13.999	1.00	23.36
ATOM	1105	CB	ASN	143	19.531	11.547	13.225	1.00	22.79
ATOM	1106	CG	ASN	143	20.055	12.906	12.826	1.00	26.55
ATOM	1107	OD1	ASN	143	20.119	13.240	11.644	1.00	29.98
ATOM	1108	ND2	ASN	143	20.442	13.697	13.815	1.00	24.11
ATOM	1109	C	ASN	143	19.928	9.461	14.543	1.00	22.26
ATOM	1110	O	ASN	143	19.689	8.519	13.798	1.00	22.91
ATOM	1111	N	LEU	144	19.667	9.438	15.846	1.00	20.92
ATOM	1112	CA	LEU	144	19.084	8.268	16.494	1.00	21.74
ATOM	1113	CB	LEU	144	19.402	8.318	17.992	1.00	18.53
ATOM	1114	CG	LEU	144	18.845	7.262	18.946	1.00	20.54
ATOM	1115	CD1	LEU	144	19.807	7.095	20.113	1.00	19.77
ATOM	1116	CD2	LEU	144	17.463	7.673	19.440	1.00	21.20
ATOM	1117	C	LEU	144	17.580	8.140	16.258	1.00	20.47
ATOM	1118	O	LEU	144	16.844	9.126	16.319	1.00	19.22
ATOM	1119	N	LYS	145	17.140	6.909	16.000	1.00	19.53
ATOM	1120	CA	LYS	145	15.737	6.605	15.730	1.00	18.88
ATOM	1121	CB	LYS	145	15.549	6.245	14.251	1.00	24.21
ATOM	1122	CG	LYS	145	16.214	7.188	13.260	1.00	23.93
ATOM	1123	CD	LYS	145	15.328	8.369	12.951	1.00	22.67
ATOM	1124	CE	LYS	145	15.970	9.275	11.913	1.00	27.57
ATOM	1125	NZ	LYS	145	15.022	10.333	11.462	1.00	27.78
ATOM	1126	C	LYS	145	15.302	5.398	16.556	1.00	15.99
ATOM	1127	O	LYS	145	15.869	4.314	16.414	1.00	16.13
ATOM	1128	N	ILE	146	14.300	5.579	17.410	1.00	16.28
ATOM	1129	CA	ILE	146	13.801	4.478	18.226	1.00	15.84
ATOM	1130	CB	ILE	146	12.849	4.993	19.319	1.00	15.02
ATOM	1131	CG2	ILE	146	12.230	3.819	20.080	1.00	13.88
ATOM	1132	CG1	ILE	146	13.635	5.884	20.284	1.00	17.67
ATOM	1133	CD1	ILE	146	12.781	6.595	21.324	1.00	12.64
ATOM	1134	C	ILE	146	13.068	3.523	17.284	1.00	16.96

FIG.11A-27

ATOM	1135	O	ILE	146	12.200	3.942	16.512	1.00	17.32
ATOM	1136	N	SER	147	13.417	2.245	17.375	1.00	16.60
ATOM	1137	CA	SER	147	12.876	1.212	16.495	1.00	17.35
ATOM	1138	CB	SER	147	14.016	0.692	15.618	1.00	16.68
ATOM	1139	OG	SER	147	13.617	-0.411	14.821	1.00	20.69
ATOM	1140	C	SER	147	12.200	0.017	17.162	1.00	16.72
ATOM	1141	O	SER	147	12.504	-0.329	18.306	1.00	15.17
ATOM	1142	N	ASP	148	11.286	-0.602	16.414	1.00	16.05
ATOM	1143	CA	ASP	148	10.549	-1.801	16.828	1.00	18.00
ATOM	1144	CB	ASP	148	11.536	-2.919	17.200	1.00	20.31
ATOM	1145	CG	ASP	148	10.874	-4.287	17.287	1.00	25.87
ATOM	1146	OD1	ASP	148	11.601	-5.305	17.231	1.00	29.19
ATOM	1147	OD2	ASP	148	9.635	-4.349	17.419	1.00	24.90
ATOM	1148	C	ASP	148	9.539	-1.618	17.951	1.00	18.24
ATOM	1149	O	ASP	148	9.887	-1.668	19.130	1.00	20.08
ATOM	1150	N	PHE	149	8.276	-1.446	17.576	1.00	18.32
ATOM	1151	CA	PHE	149	7.218	-1.265	18.554	1.00	19.50
ATOM	1152	CB	PHE	149	6.346	-0.077	18.152	1.00	17.84
ATOM	1153	CG	PHE	149	7.065	1.232	18.263	1.00	19.16
ATOM	1154	CD1	PHE	149	7.955	1.637	17.271	1.00	19.71
ATOM	1155	CD2	PHE	149	6.932	2.014	19.407	1.00	15.99
ATOM	1156	CE1	PHE	149	8.712	2.805	17.418	1.00	19.45
ATOM	1157	CE2	PHE	149	7.687	3.184	19.564	1.00	20.50
ATOM	1158	CZ	PHE	149	8.576	3.576	18.568	1.00	19.86
ATOM	1159	C	PHE	149	6.391	-2.516	18.780	1.00	20.77
ATOM	1160	O	PHE	149	5.235	-2.445	19.187	1.00	21.42
ATOM	1161	N	GLY	150	7.020	-3.663	18.539	1.00	20.98
ATOM	1162	CA	GLY	150	6.361	-4.942	18.725	1.00	21.69
ATOM	1163	C	GLY	150	6.002	-5.220	20.176	1.00	21.45
ATOM	1164	O	GLY	150	5.111	-6.018	20.449	1.00	24.57
ATOM	1165	N	LEU	151	6.687	-4.568	21.111	1.00	19.98
ATOM	1166	CA	LEU	151	6.396	-4.763	22.535	1.00	21.36
ATOM	1167	CB	LEU	151	7.659	-5.180	23.289	1.00	18.98
ATOM	1168	CG	LEU	151	8.189	-6.589	23.004	1.00	24.33
ATOM	1169	CD1	LEU	151	9.497	-6.797	23.744	1.00	25.19
ATOM	1170	CD2	LEU	151	7.153	-7.628	23.440	1.00	27.70
ATOM	1171	C	LEU	151	5.811	-3.520	23.195	1.00	19.87
ATOM	1172	O	LEU	151	5.517	-3.530	24.389	1.00	20.65
ATOM	1173	N	ALA	152	5.640	-2.458	22.413	1.00	18.07
ATOM	1174	CA	ALA	152	5.102	-1.199	22.915	1.00	18.82
ATOM	1175	CB	ALA	152	5.296	-0.103	21.867	1.00	16.88
ATOM	1176	C	ALA	152	3.627	-1.290	23.285	1.00	19.46

FIG.11A-28

ATOM	1177	O	ALA	152	2.895	-2.129	22.758	1.00	21.66
ATOM	1178	N	THR	153	3.192	-0.418	24.189	1.00	19.05
ATOM	1179	CA	THR	153	1.796	-0.397	24.593	1.00	18.72
ATOM	1180	CB	THR	153	1.509	-1.442	25.712	1.00	18.18
ATOM	1181	OG1	THR	153	0.090	-1.652	25.809	1.00	16.70
ATOM	1182	CG2	THR	153	2.038	-0.970	27.071	1.00	16.94
ATOM	1183	C	THR	153	1.396	1.000	25.056	1.00	19.47
ATOM	1184	O	THR	153	2.244	1.853	25.325	1.00	17.58
ATOM	1185	N	VAL	154	0.096	1.249	25.112	1.00	21.41
ATOM	1186	CA	VAL	154	-0.401	2.543	25.547	1.00	22.13
ATOM	1187	CB	VAL	154	-1.765	2.863	24.877	1.00	26.46
ATOM	1188	CG1	VAL	154	-2.295	4.213	25.354	1.00	28.65
ATOM	1189	CG2	VAL	154	-1.600	2.873	23.367	1.00	24.98
ATOM	1190	C	VAL	154	-0.559	2.472	27.056	1.00	21.16
ATOM	1191	O	VAL	154	-1.195	1.553	27.577	1.00	21.97
ATOM	1192	N	PHE	155	0.047	3.416	27.770	1.00	19.24
ATOM	1193	CA	PHE	155	-0.061	3.414	29.220	1.00	18.72
ATOM	1194	CB	PHE	155	1.322	3.426	29.889	1.00	19.67
ATOM	1195	CG	PHE	155	2.055	4.721	29.748	1.00	17.34
ATOM	1196	CD1	PHE	155	2.843	4.972	28.628	1.00	13.52
ATOM	1197	CD2	PHE	155	1.924	5.711	30.716	1.00	16.84
ATOM	1198	CE1	PHE	155	3.488	6.191	28.470	1.00	13.59
ATOM	1199	CE2	PHE	155	2.565	6.944	30.570	1.00	16.30
ATOM	1200	CZ	PHE	155	3.350	7.187	29.445	1.00	15.78
ATOM	1201	C	PHE	155	-0.889	4.590	29.717	1.00	20.17
ATOM	1202	O	PHE	155	-1.170	4.696	30.907	1.00	20.34
ATOM	1203	N	ARG	156	-1.259	5.489	28.812	1.00	19.17
ATOM	1204	CA	ARG	156	-2.096	6.622	29.204	1.00	18.98
ATOM	1205	CB	ARG	156	-1.282	7.904	29.388	1.00	17.96
ATOM	1206	CG	ARG	156	-2.081	9.008	30.101	1.00	20.91
ATOM	1207	CD	ARG	156	-1.432	10.382	29.971	1.00	26.19
ATOM	1208	NE	ARG	156	-0.049	10.410	30.438	1.00	25.61
ATOM	1209	CZ	ARG	156	1.002	10.600	29.642	1.00	20.60
ATOM	1210	NH1	ARG	156	0.830	10.774	28.340	1.00	19.60
ATOM	1211	NH2	ARG	156	2.226	10.628	30.150	1.00	18.11
ATOM	1212	C	ARG	156	-3.134	6.847	28.122	1.00	21.82
ATOM	1213	O	ARG	156	-2.802	7.039	26.954	1.00	21.83
ATOM	1214	N	TYR	157	-4.398	6.824	28.521	1.00	21.32
ATOM	1215	CA	TYR	157	-5.493	7.016	27.584	1.00	19.71
ATOM	1216	CB	TYR	157	-6.101	5.663	27.218	1.00	18.64
ATOM	1217	CG	TYR	157	-6.960	5.702	25.983	1.00	23.71
ATOM	1218	CD1	TYR	157	-6.384	5.726	24.712	1.00	21.76

FIG.11A-29

ATOM	1219	CE1	TYR	157	-7.174	5.767	23.566	1.00	25.10
ATOM	1220	CD2	TYR	157	-8.350	5.719	26.081	1.00	19.65
ATOM	1221	CE2	TYR	157	-9.147	5.756	24.946	1.00	19.21
ATOM	1222	CZ	TYR	157	-8.559	5.780	23.693	1.00	22.17
ATOM	1223	OH	TYR	157	-9.347	5.818	22.566	1.00	25.91
ATOM	1224	C	TYR	157	-6.533	7.882	28.282	1.00	18.10
ATOM	1225	O	TYR	157	-6.851	7.651	29.449	1.00	18.79
ATOM	1226	N	ASN	158	-7.045	8.881	27.571	1.00	19.43
ATOM	1227	CA	ASN	158	-8.041	9.797	28.130	1.00	22.45
ATOM	1228	CB	ASN	158	-9.375	9.068	28.342	1.00	17.95
ATOM	1229	CG	ASN	158	-10.134	8.861	27.046	1.00	15.00
ATOM	1230	OD1	ASN	158	-11.036	8.025	26.968	1.00	21.50
ATOM	1231	ND2	ASN	158	-9.777	9.620	26.018	1.00	14.33
ATOM	1232	C	ASN	158	-7.565	10.417	29.442	1.00	24.59
ATOM	1233	O	ASN	158	-8.339	10.591	30.383	1.00	25.26
ATOM	1234	N	ASN	159	-6.272	10.731	29.482	1.00	27.27
ATOM	1235	CA	ASN	159	-5.624	11.353	30.630	1.00	28.47
ATOM	1236	CB	ASN	159	-6.285	12.702	30.934	1.00	34.81
ATOM	1237	CG	ASN	159	-5.380	13.624	31.730	1.00	46.84
ATOM	1238	OD1	ASN	159	-4.243	13.884	31.332	1.00	48.82
ATOM	1239	ND2	ASN	159	-5.880	14.126	32.856	1.00	48.82
ATOM	1240	C	ASN	159	-5.597	10.489	31.889	1.00	27.91
ATOM	1241	O	ASN	159	-5.381	10.991	32.993	1.00	30.07
ATOM	1242	N	ARG	160	-5.818	9.189	31.725	1.00	24.35
ATOM	1243	CA	ARG	160	-5.788	8.265	32.854	1.00	23.07
ATOM	1244	CB	ARG	160	-7.104	7.485	32.961	1.00	24.32
ATOM	1245	CG	ARG	160	-8.050	7.997	34.040	1.00	31.06
ATOM	1246	CD	ARG	160	-7.472	7.775	35.429	1.00	36.21
ATOM	1247	NE	ARG	160	-8.462	7.992	36.479	1.00	49.83
ATOM	1248	CZ	ARG	160	-8.983	9.174	36.791	1.00	58.03
ATOM	1249	NH1	ARG	160	-8.608	10.264	36.135	1.00	61.87
ATOM	1250	NH2	ARG	160	-9.887	9.265	37.758	1.00	59.82
ATOM	1251	C	ARG	160	-4.639	7.289	32.648	1.00	22.67
ATOM	1252	O	ARG	160	-4.562	6.628	31.618	1.00	20.87
ATOM	1253	N	GLU	161	-3.750	7.204	33.630	1.00	22.22
ATOM	1254	CA	GLU	161	-2.613	6.298	33.527	1.00	22.53
ATOM	1255	CB	GLU	161	-1.459	6.768	34.429	1.00	22.92
ATOM	1256	CG	GLU	161	-0.214	5.877	34.340	1.00	21.95
ATOM	1257	CD	GLU	161	0.902	6.279	35.305	1.00	24.35
ATOM	1258	OE1	GLU	161	1.976	5.637	35.272	1.00	20.96
ATOM	1259	OE2	GLU	161	0.706	7.226	36.095	1.00	25.52
ATOM	1260	C	GLU	161	-3.007	4.885	33.926	1.00	21.71

FIG.11A-30

ATOM	1261	O	GLU	161	-3.755	4.683	34.885	1.00	23.04
ATOM	1262	N	ARG	162	-2.503	3.909	33.182	1.00	21.16
ATOM	1263	CA	ARG	162	-2.754	2.505	33.465	1.00	21.51
ATOM	1264	CB	ARG	162	-3.207	1.781	32.191	1.00	26.46
ATOM	1265	CG	ARG	162	-3.326	0.274	32.326	1.00	33.90
ATOM	1266	CD	ARG	162	-3.916	-0.347	31.061	1.00	44.41
ATOM	1267	NE	ARG	162	-3.035	-0.230	29.898	1.00	54.96
ATOM	1268	CZ	ARG	162	-2.050	-1.077	29.612	1.00	52.17
ATOM	1269	NH1	ARG	162	-1.303	-0.884	28.534	1.00	48.31
ATOM	1270	NH2	ARG	162	-1.816	-2.123	30.392	1.00	49.02
ATOM	1271	C	ARG	162	-1.442	1.892	33.957	1.00	21.44
ATOM	1272	O	ARG	162	-0.405	2.058	33.319	1.00	20.36
ATOM	1273	N	LEU	163	-1.481	1.215	35.098	1.00	20.22
ATOM	1274	CA	LEU	163	-0.279	0.573	35.623	1.00	21.99
ATOM	1275	CB	LEU	163	-0.448	0.226	37.100	1.00	22.03
ATOM	1276	CG	LEU	163	-0.661	1.398	38.057	1.00	23.54
ATOM	1277	CD1	LEU	163	-1.002	0.862	39.439	1.00	21.82
ATOM	1278	CD2	LEU	163	0.598	2.269	38.100	1.00	23.24
ATOM	1279	C	LEU	163	-0.051	-0.699	34.823	1.00	22.61
ATOM	1280	O	LEU	163	-1.000	-1.362	34.411	1.00	23.66
ATOM	1281	N	LEU	164	1.211	-1.045	34.604	1.00	21.45
ATOM	1282	CA	LEU	164	1.526	-2.245	33.839	1.00	19.50
ATOM	1283	CB	LEU	164	2.699	-1.966	32.898	1.00	19.82
ATOM	1284	CG	LEU	164	2.524	-0.748	31.991	1.00	21.21
ATOM	1285	CD1	LEU	164	3.741	-0.606	31.096	1.00	23.59
ATOM	1286	CD2	LEU	164	1.260	-0.897	31.166	1.00	21.35
ATOM	1287	C	LEU	164	1.887	-3.402	34.752	1.00	17.33
ATOM	1288	O	LEU	164	2.254	-3.194	35.909	1.00	16.78
ATOM	1289	N	ASN	165	1.784	-4.621	34.222	1.00	17.32
ATOM	1290	CA	ASN	165	2.139	-5.818	34.978	1.00	19.46
ATOM	1291	CB	ASN	165	0.898	-6.443	35.622	1.00	22.03
ATOM	1292	CG	ASN	165	-0.189	-6.740	34.611	1.00	24.96
ATOM	1293	OD1	ASN	165	-1.219	-6.065	34.574	1.00	31.70
ATOM	1294	ND2	ASN	165	0.037	-7.748	33.776	1.00	22.31
ATOM	1295	C	ASN	165	2.816	-6.855	34.084	1.00	19.59
ATOM	1296	O	ASN	165	3.349	-7.849	34.569	1.00	21.55
ATOM	1297	N	LYS	166	2.804	-6.625	32.778	1.00	20.65
ATOM	1298	CA	LYS	166	3.425	-7.570	31.854	1.00	23.25
ATOM	1299	CB	LYS	166	3.029	-7.232	30.414	1.00	25.58
ATOM	1300	CG	LYS	166	3.605	-8.164	29.356	1.00	28.68
ATOM	1301	CD	LYS	166	3.109	-7.776	27.968	1.00	34.56
ATOM	1302	CE	LYS	166	3.602	-8.742	26.904	1.00	40.12

FIG.11A-31

ATOM	1303	NZ	LYS	166	5.089	-8.750	26.811	1.00	47.83
ATOM	1304	C	LYS	166	4.949	-7.569	31.982	1.00	22.75
ATOM	1305	O	LYS	166	5.594	-6.523	31.884	1.00	20.68
ATOM	1306	N	MET	167	5.523	-8.741	32.230	1.00	22.74
ATOM	1307	CA	MET	167	6.973	-8.835	32.320	1.00	23.09
ATOM	1308	CB	MET	167	7.404	-10.040	33.163	1.00	24.13
ATOM	1309	CG	MET	167	7.362	-9.790	34.665	1.00	24.94
ATOM	1310	SD	MET	167	8.034	-11.177	35.618	1.00	44.99
ATOM	1311	CE	MET	167	6.628	-12.283	35.657	1.00	40.11
ATOM	1312	C	MET	167	7.472	-8.985	30.891	1.00	23.61
ATOM	1313	O	MET	167	7.164	-9.962	30.213	1.00	24.88
ATOM	1314	N	CYS	168	8.214	-7.989	30.424	1.00	19.83
ATOM	1315	CA	CYS	168	8.744	-8.018	29.071	1.00	19.64
ATOM	1316	CB	CYS	168	7.687	-7.578	28.061	1.00	19.32
ATOM	1317	SG	CYS	168	6.981	-5.932	28.333	1.00	25.33
ATOM	1318	C	CYS	168	9.959	-7.112	28.979	1.00	19.48
ATOM	1319	O	CYS	168	10.243	-6.341	29.899	1.00	19.57
ATOM	1320	N	GLY	169	10.668	-7.212	27.860	1.00	18.34
ATOM	1321	CA	GLY	169	11.867	-6.422	27.671	1.00	16.84
ATOM	1322	C	GLY	169	13.056	-7.347	27.473	1.00	17.86
ATOM	1323	O	GLY	169	12.910	-8.446	26.932	1.00	17.29
ATOM	1324	N	THR	170	14.225	-6.898	27.922	1.00	16.83
ATOM	1325	CA	THR	170	15.473	-7.649	27.811	1.00	17.19
ATOM	1326	CB	THR	170	16.343	-7.057	26.678	1.00	16.59
ATOM	1327	OG1	THR	170	15.593	-7.087	25.453	1.00	16.29
ATOM	1328	CG2	THR	170	17.606	-7.871	26.483	1.00	17.54
ATOM	1329	C	THR	170	16.160	-7.520	29.176	1.00	15.39
ATOM	1330	O	THR	170	16.494	-6.416	29.608	1.00	13.60
ATOM	1331	N	LEU	171	16.374	-8.658	29.838	1.00	15.78
ATOM	1332	CA	LEU	171	16.938	-8.697	31.190	1.00	15.62
ATOM	1333	CB	LEU	171	17.420	-10.126	31.494	1.00	17.62
ATOM	1334	CG	LEU	171	16.781	-10.963	32.621	1.00	24.25
ATOM	1335	CD1	LEU	171	15.469	-10.373	33.131	1.00	20.87
ATOM	1336	CD2	LEU	171	16.577	-12.390	32.116	1.00	14.78
ATOM	1337	C	LEU	171	18.007	-7.675	31.615	1.00	15.63
ATOM	1338	O	LEU	171	17.835	-6.989	32.625	1.00	14.39
ATOM	1339	N	PRO	172	19.123	-7.559	30.872	1.00	15.88
ATOM	1340	CD	PRO	172	19.564	-8.355	29.713	1.00	18.04
ATOM	1341	CA	PRO	172	20.156	-6.589	31.270	1.00	16.57
ATOM	1342	CB	PRO	172	21.268	-6.815	30.244	1.00	16.20
ATOM	1343	CG	PRO	172	21.060	-8.248	29.811	1.00	17.53
ATOM	1344	C	PRO	172	19.689	-5.133	31.284	1.00	16.25

FIG.11A-32

ATOM	1345	O	PRO	172	20.268	-4.291	31.972	1.00	18.87
ATOM	1346	N	TYR	173	18.630	-4.852	30.532	1.00	15.37
ATOM	1347	CA	TYR	173	18.073	-3.506	30.421	1.00	14.75
ATOM	1348	CB	TYR	173	17.757	-3.218	28.950	1.00	13.39
ATOM	1349	CG	TYR	173	18.954	-3.298	28.046	1.00	14.82
ATOM	1350	CD1	TYR	173	19.745	-2.182	27.811	1.00	15.47
ATOM	1351	CE1	TYR	173	20.872	-2.255	26.993	1.00	20.45
ATOM	1352	CD2	TYR	173	19.314	-4.503	27.438	1.00	19.99
ATOM	1353	CE2	TYR	173	20.435	-4.585	26.617	1.00	23.28
ATOM	1354	CZ	TYR	173	21.208	-3.455	26.401	1.00	20.15
ATOM	1355	OH	TYR	173	22.317	-3.523	25.586	1.00	23.35
ATOM	1356	C	TYR	173	16.795	-3.271	31.223	1.00	14.06
ATOM	1357	O	TYR	173	16.336	-2.135	31.351	1.00	13.16
ATOM	1358	N	VAL	174	16.212	-4.328	31.771	1.00	15.36
ATOM	1359	CA	VAL	174	14.950	-4.171	32.485	1.00	15.69
ATOM	1360	CB	VAL	174	14.183	-5.529	32.498	1.00	18.37
ATOM	1361	CG1	VAL	174	14.686	-6.421	33.634	1.00	16.95
ATOM	1362	CG2	VAL	174	12.689	-5.284	32.590	1.00	20.81
ATOM	1363	C	VAL	174	15.083	-3.596	33.909	1.00	14.76
ATOM	1364	O	VAL	174	16.048	-3.875	34.616	1.00	14.52
ATOM	1365	N	ALA	175	14.109	-2.778	34.302	1.00	14.40
ATOM	1366	CA	ALA	175	14.099	-2.152	35.628	1.00	14.61
ATOM	1367	CB	ALA	175	13.044	-1.055	35.669	1.00	15.96
ATOM	1368	C	ALA	175	13.830	-3.185	36.729	1.00	14.55
ATOM	1369	O	ALA	175	13.079	-4.130	36.529	1.00	14.73
ATOM	1370	N	PRO	176	14.435	-3.001	37.912	1.00	14.46
ATOM	1371	CD	PRO	176	15.321	-1.891	38.303	1.00	16.61
ATOM	1372	CA	PRO	176	14.247	-3.941	39.022	1.00	15.95
ATOM	1373	CB	PRO	176	15.154	-3.372	40.120	1.00	18.53
ATOM	1374	CG	PRO	176	15.200	-1.896	39.812	1.00	17.80
ATOM	1375	C	PRO	176	12.805	-4.157	39.487	1.00	17.01
ATOM	1376	O	PRO	176	12.456	-5.257	39.923	1.00	18.04
ATOM	1377	N	GLU	177	11.958	-3.134	39.381	1.00	17.70
ATOM	1378	CA	GLU	177	10.578	-3.294	39.819	1.00	19.33
ATOM	1379	CB	GLU	177	9.831	-1.954	39.825	1.00	19.43
ATOM	1380	CG	GLU	177	9.711	-1.238	38.479	1.00	18.24
ATOM	1381	CD	GLU	177	10.866	-0.291	38.199	1.00	18.08
ATOM	1382	OE1	GLU	177	10.672	0.643	37.389	1.00	15.25
ATOM	1383	OE2	GLU	177	11.962	-0.481	38.775	1.00	19.51
ATOM	1384	C	GLU	177	9.815	-4.314	38.977	1.00	19.97
ATOM	1385	O	GLU	177	8.877	-4.941	39.455	1.00	18.86
ATOM	1386	N	LEU	178	10.214	-4.485	37.721	1.00	18.60

FIG.11A-33

ATOM	1387	CA	LEU	178	9.540	-5.448	36.861	1.00	21.80
ATOM	1388	CB	LEU	178	10.037	-5.283	35.412	1.00	26.36
ATOM	1389	CG	LEU	178	9.551	-6.196	34.281	1.00	30.81
ATOM	1390	CD1	LEU	178	10.271	-7.531	34.349	1.00	32.00
ATOM	1391	CD2	LEU	178	8.053	-6.389	34.371	1.00	34.42
ATOM	1392	C	LEU	178	9.789	-6.866	37.379	1.00	21.49
ATOM	1393	O	LEU	178	8.987	-7.776	37.148	1.00	22.54
ATOM	1394	N	LEU	179	10.886	-7.051	38.107	1.00	22.22
ATOM	1395	CA	LEU	179	11.213	-8.365	38.648	1.00	23.39
ATOM	1396	CB	LEU	179	12.719	-8.621	38.558	1.00	23.03
ATOM	1397	CG	LEU	179	13.416	-8.495	37.200	1.00	26.29
ATOM	1398	CD1	LEU	179	14.903	-8.733	37.390	1.00	24.67
ATOM	1399	CD2	LEU	179	12.837	-9.491	36.204	1.00	26.57
ATOM	1400	C	LEU	179	10.770	-8.558	40.096	1.00	24.84
ATOM	1401	O	LEU	179	10.847	-9.667	40.627	1.00	26.92
ATOM	1402	N	LYS	180	10.295	-7.504	40.746	1.00	23.35
ATOM	1403	CA	LYS	180	9.908	-7.666	42.143	1.00	25.69
ATOM	1404	CB	LYS	180	10.916	-6.949	43.044	1.00	31.39
ATOM	1405	CG	LYS	180	11.002	-5.452	42.823	1.00	40.61
ATOM	1406	CD	LYS	180	12.048	-4.816	43.737	1.00	49.38
ATOM	1407	CE	LYS	180	13.441	-5.362	43.457	1.00	56.38
ATOM	1408	NZ	LYS	180	14.482	-4.726	44.313	1.00	63.75
ATOM	1409	C	LYS	180	8.508	-7.228	42.521	1.00	26.89
ATOM	1410	O	LYS	180	8.025	-7.586	43.596	1.00	27.55
ATOM	1411	N	ARG	181	7.849	-6.471	41.651	1.00	25.95
ATOM	1412	CA	ARG	181	6.507	-5.985	41.953	1.00	23.62
ATOM	1413	CB	ARG	181	6.515	-4.457	42.013	1.00	20.86
ATOM	1414	CG	ARG	181	7.886	-3.864	42.345	1.00	23.41
ATOM	1415	CD	ARG	181	7.952	-3.096	43.655	1.00	28.25
ATOM	1416	NE	ARG	181	7.769	-3.932	44.835	1.00	26.30
ATOM	1417	CZ	ARG	181	8.303	-3.678	46.032	1.00	25.03
ATOM	1418	NH1	ARG	181	8.059	-4.494	47.048	1.00	21.28
ATOM	1419	NH2	ARG	181	9.096	-2.632	46.221	1.00	26.39
ATOM	1420	C	ARG	181	5.489	-6.459	40.921	1.00	24.18
ATOM	1421	O	ARG	181	5.813	-6.625	39.743	1.00	23.59
ATOM	1422	N	ARG	182	4.257	-6.685	41.362	1.00	26.62
ATOM	1423	CA	ARG	182	3.214	-7.141	40.452	1.00	27.87
ATOM	1424	CB	ARG	182	1.958	-7.550	41.229	1.00	32.39
ATOM	1425	CG	ARG	182	0.955	-8.322	40.382	1.00	45.18
ATOM	1426	CD	ARG	182	-0.386	-8.462	41.083	1.00	54.85
ATOM	1427	NE	ARG	182	-1.032	-7.166	41.265	1.00	60.82
ATOM	1428	CZ	ARG	182	-2.245	-6.998	41.781	1.00	66.47

FIG.11A-34

ATOM	1429	NH1	ARG	182	-2.954	-8.049	42.170	1.00	73.47
ATOM	1430	NH2	ARG	182	-2.750	-5.778	41.905	1.00	66.10
ATOM	1431	C	ARG	182	2.852	-6.046	39.450	1.00	25.07
ATOM	1432	O	ARG	182	2.667	-6.320	38.261	1.00	25.61
ATOM	1433	N	GLU	183	2.744	-4.812	39.936	1.00	23.08
ATOM	1434	CA	GLU	183	2.406	-3.673	39.085	1.00	23.45
ATOM	1435	CB	GLU	183	1.067	-3.059	39.501	1.00	21.25
ATOM	1436	CG	GLU	183	-0.147	-3.899	39.187	1.00	24.48
ATOM	1437	CD	GLU	183	-1.423	-3.181	39.569	1.00	30.66
ATOM	1438	OE1	GLU	183	-1.611	-2.902	40.771	1.00	34.79
ATOM	1439	OE2	GLU	183	-2.228	-2.883	38.666	1.00	30.34
ATOM	1440	C	GLU	183	3.482	-2.600	39.169	1.00	21.06
ATOM	1441	O	GLU	183	4.209	-2.512	40.158	1.00	21.34
ATOM	1442	N	PHE	184	3.565	-1.768	38.137	1.00	18.15
ATOM	1443	CA	PHE	184	4.567	-0.717	38.105	1.00	15.58
ATOM	1444	CB	PHE	184	5.945	-1.346	37.819	1.00	16.74
ATOM	1445	CG	PHE	184	5.926	-2.381	36.726	1.00	14.62
ATOM	1446	CD1	PHE	184	5.951	-2.005	35.392	1.00	18.17
ATOM	1447	CD2	PHE	184	5.815	-3.739	37.036	1.00	17.28
ATOM	1448	CE1	PHE	184	5.860	-2.959	34.375	1.00	20.20
ATOM	1449	CE2	PHE	184	5.721	-4.698	36.029	1.00	16.96
ATOM	1450	CZ	PHE	184	5.741	-4.306	34.696	1.00	17.04
ATOM	1451	C	PHE	184	4.222	0.353	37.067	1.00	16.19
ATOM	1452	O	PHE	184	3.506	0.084	36.096	1.00	15.45
ATOM	1453	N	HIS	185	4.707	1.569	37.298	1.00	16.14
ATOM	1454	CA	HIS	185	4.499	2.688	36.380	1.00	17.03
ATOM	1455	CB	HIS	185	4.911	3.998	37.057	1.00	15.20
ATOM	1456	CG	HIS	185	3.954	4.462	38.110	1.00	17.47
ATOM	1457	CD2	HIS	185	4.016	4.403	39.463	1.00	16.97
ATOM	1458	ND1	HIS	185	2.755	5.074	37.808	1.00	17.76
ATOM	1459	CE1	HIS	185	2.122	5.373	38.930	1.00	15.00
ATOM	1460	NE2	HIS	185	2.866	4.978	39.948	1.00	16.42
ATOM	1461	C	HIS	185	5.346	2.468	35.121	1.00	16.88
ATOM	1462	O	HIS	185	6.489	2.023	35.202	1.00	15.15
ATOM	1463	N	ALA	186	4.789	2.789	33.959	1.00	15.23
ATOM	1464	CA	ALA	186	5.500	2.584	32.696	1.00	14.49
ATOM	1465	CB	ALA	186	4.543	2.773	31.529	1.00	11.65
ATOM	1466	C	ALA	186	6.719	3.472	32.469	1.00	15.84
ATOM	1467	O	ALA	186	7.768	2.999	32.039	1.00	13.75
ATOM	1468	N	GLU	187	6.579	4.760	32.747	1.00	13.01
ATOM	1469	CA	GLU	187	7.665	5.694	32.475	1.00	14.78
ATOM	1470	CB	GLU	187	7.190	7.118	32.758	1.00	13.83

FIG.11A-35

ATOM	1471	CG	GLU	187	6.131	7.564	31.755	1.00	14.84
ATOM	1472	CD	GLU	187	5.476	8.860	32.155	1.00	17.06
ATOM	1473	OE1	GLU	187	5.783	9.898	31.537	1.00	17.90
ATOM	1474	OE2	GLU	187	4.669	8.836	33.101	1.00	25.47
ATOM	1475	C	GLU	187	9.023	5.420	33.119	1.00	13.36
ATOM	1476	O	GLU	187	10.044	5.468	32.435	1.00	14.03
ATOM	1477	N	PRO	188	9.064	5.134	34.427	1.00	12.65
ATOM	1478	CD	PRO	188	8.004	5.222	35.448	1.00	12.15
ATOM	1479	CA	PRO	188	10.369	4.868	35.042	1.00	11.62
ATOM	1480	CB	PRO	188	10.029	4.690	36.532	1.00	13.87
ATOM	1481	CG	PRO	188	8.799	5.543	36.707	1.00	12.10
ATOM	1482	C	PRO	188	11.079	3.639	34.471	1.00	11.69
ATOM	1483	O	PRO	188	12.302	3.525	34.575	1.00	13.08
ATOM	1484	N	VAL	189	10.324	2.709	33.878	1.00	12.14
ATOM	1485	CA	VAL	189	10.934	1.508	33.313	1.00	12.36
ATOM	1486	CB	VAL	189	9.845	0.440	32.946	1.00	11.17
ATOM	1487	CG1	VAL	189	10.485	-0.758	32.243	1.00	11.29
ATOM	1488	CG2	VAL	189	9.135	-0.030	34.207	1.00	12.20
ATOM	1489	C	VAL	189	11.746	1.907	32.069	1.00	14.29
ATOM	1490	O	VAL	189	12.877	1.442	31.873	1.00	13.97
ATOM	1491	N	ASP	190	11.180	2.781	31.237	1.00	13.89
ATOM	1492	CA	ASP	190	11.882	3.237	30.042	1.00	13.47
ATOM	1493	CB	ASP	190	10.952	4.039	29.115	1.00	15.20
ATOM	1494	CG	ASP	190	10.078	3.154	28.230	1.00	17.71
ATOM	1495	OD1	ASP	190	10.434	1.981	27.987	1.00	16.91
ATOM	1496	OD2	ASP	190	9.037	3.652	27.754	1.00	17.19
ATOM	1497	C	ASP	190	13.062	4.124	30.462	1.00	13.29
ATOM	1498	O	ASP	190	14.109	4.135	29.820	1.00	11.95
ATOM	1499	N	VAL	191	12.903	4.870	31.547	1.00	13.34
ATOM	1500	CA	VAL	191	14.009	5.716	31.988	1.00	14.45
ATOM	1501	CB	VAL	191	13.602	6.603	33.187	1.00	14.74
ATOM	1502	CG1	VAL	191	14.842	7.202	33.852	1.00	12.70
ATOM	1503	CG2	VAL	191	12.688	7.727	32.692	1.00	13.03
ATOM	1504	C	VAL	191	15.203	4.840	32.386	1.00	13.08
ATOM	1505	O	VAL	191	16.346	5.146	32.053	1.00	11.25
ATOM	1506	N	TRP	192	14.921	3.756	33.094	1.00	12.71
ATOM	1507	CA	TRP	192	15.958	2.833	33.546	1.00	12.03
ATOM	1508	CB	TRP	192	15.322	1.727	34.409	1.00	9.46
ATOM	1509	CG	TRP	192	16.294	0.677	34.852	1.00	12.75
ATOM	1510	CD2	TRP	192	16.899	0.563	36.145	1.00	13.79
ATOM	1511	CE2	TRP	192	17.767	-0.550	36.104	1.00	11.39
ATOM	1512	CE3	TRP	192	16.789	1.294	37.338	1.00	12.63

FIG.11A-36

ATOM	1513	CD1	TRP	192	16.804	-0.342	34.098	1.00	12.01
ATOM	1514	NE1	TRP	192	17.691	-1.086	34.846	1.00	12.49
ATOM	1515	CZ2	TRP	192	18.525	-0.952	37.215	1.00	12.51
ATOM	1516	CZ3	TRP	192	17.537	0.894	38.439	1.00	14.40
ATOM	1517	CH2	TRP	192	18.396	-0.221	38.368	1.00	12.56
ATOM	1518	C	TRP	192	16.713	2.226	32.364	1.00	12.79
ATOM	1519	O	TRP	192	17.947	2.240	32.345	1.00	12.82
ATOM	1520	N	SER	193	15.991	1.706	31.373	1.00	13.03
ATOM	1521	CA	SER	193	16.676	1.118	30.221	1.00	13.36
ATOM	1522	CB	SER	193	15.672	0.467	29.263	1.00	11.41
ATOM	1523	OG	SER	193	14.658	1.368	28.864	1.00	14.36
ATOM	1524	C	SER	193	17.523	2.175	29.506	1.00	13.32
ATOM	1525	O	SER	193	18.582	1.866	28.973	1.00	12.69
ATOM	1526	N	CYS	194	17.064	3.420	29.471	1.00	12.77
ATOM	1527	CA	CYS	194	17.886	4.463	28.840	1.00	13.01
ATOM	1528	CB	CYS	194	17.136	5.799	28.793	1.00	11.84
ATOM	1529	SG	CYS	194	15.813	5.829	27.558	1.00	12.71
ATOM	1530	C	CYS	194	19.195	4.643	29.624	1.00	11.67
ATOM	1531	O	CYS	194	20.223	4.970	29.050	1.00	13.09
ATOM	1532	N	GLY	195	19.137	4.424	30.934	1.00	11.41
ATOM	1533	CA	GLY	195	20.324	4.541	31.776	1.00	12.03
ATOM	1534	C	GLY	195	21.311	3.421	31.480	1.00	12.90
ATOM	1535	O	GLY	195	22.529	3.624	31.491	1.00	12.32
ATOM	1536	N	ILE	196	20.792	2.225	31.223	1.00	13.85
ATOM	1537	CA	ILE	196	21.673	1.100	30.899	1.00	15.56
ATOM	1538	CB	ILE	196	20.896	-0.240	30.942	1.00	21.20
ATOM	1539	CG2	ILE	196	19.649	-0.143	30.132	1.00	21.27
ATOM	1540	CG1	ILE	196	21.763	-1.380	30.415	1.00	20.74
ATOM	1541	CD1	ILE	196	22.970	-1.620	31.237	1.00	36.22
ATOM	1542	C	ILE	196	22.294	1.345	29.516	1.00	13.15
ATOM	1543	O	ILE	196	23.459	1.009	29.277	1.00	12.36
ATOM	1544	N	VAL	197	21.527	1.941	28.603	1.00	12.90
ATOM	1545	CA	VAL	197	22.054	2.257	27.278	1.00	13.36
ATOM	1546	CB	VAL	197	20.957	2.852	26.349	1.00	13.82
ATOM	1547	CG1	VAL	197	21.593	3.495	25.106	1.00	12.22
ATOM	1548	CG2	VAL	197	19.986	1.740	25.929	1.00	13.53
ATOM	1549	C	VAL	197	23.193	3.270	27.438	1.00	14.88
ATOM	1550	O	VAL	197	24.220	3.168	26.767	1.00	16.68
ATOM	1551	N	LEU	198	23.026	4.231	28.344	1.00	13.75
ATOM	1552	CA	LEU	198	24.060	5.244	28.561	1.00	13.15
ATOM	1553	CB	LEU	198	23.579	6.306	29.552	1.00	12.43
ATOM	1554	CG	LEU	198	23.930	7.793	29.353	1.00	21.66

FIG.11A-37

ATOM	1555	CD1	LEU	198	23.945	8.469	30.718	1.00	15.92
ATOM	1556	CD2	LEU	198	25.243	8.000	28.625	1.00	14.52
ATOM	1557	C	LEU	198	25.313	4.560	29.110	1.00	14.88
ATOM	1558	O	LEU	198	26.436	4.864	28.702	1.00	14.46
ATOM	1559	N	THR	199	25.117	3.639	30.044	1.00	14.39
ATOM	1560	CA	THR	199	26.250	2.909	30.623	1.00	16.47
ATOM	1561	CB	THR	199	25.766	1.920	31.698	1.00	14.59
ATOM	1562	OG1	THR	199	25.085	2.643	32.728	1.00	15.04
ATOM	1563	CG2	THR	199	26.947	1.174	32.321	1.00	13.58
ATOM	1564	C	THR	199	27.005	2.156	29.523	1.00	17.44
ATOM	1565	O	THR	199	28.237	2.192	29.465	1.00	18.28
ATOM	1566	N	ALA	200	26.261	1.486	28.646	1.00	15.89
ATOM	1567	CA	ALA	200	26.866	0.736	27.546	1.00	16.21
ATOM	1568	CB	ALA	200	25.777	0.003	26.749	1.00	14.29
ATOM	1569	C	ALA	200	27.662	1.660	26.623	1.00	17.57
ATOM	1570	O	ALA	200	28.781	1.337	26.225	1.00	18.68
ATOM	1571	N	MET	201	27.090	2.808	26.271	1.00	16.39
ATOM	1572	CA	MET	201	27.792	3.742	25.389	1.00	14.62
ATOM	1573	CB	MET	201	26.904	4.941	25.025	1.00	11.19
ATOM	1574	CG	MET	201	25.656	4.594	24.221	1.00	13.75
ATOM	1575	SD	MET	201	24.917	6.071	23.450	1.00	18.10
ATOM	1576	CE	MET	201	24.144	6.895	24.918	1.00	13.57
ATOM	1577	C	MET	201	29.080	4.275	26.006	1.00	15.76
ATOM	1578	O	MET	201	30.055	4.523	25.296	1.00	15.99
ATOM	1579	N	LEU	202	29.086	4.444	27.325	1.00	15.81
ATOM	1580	CA	LEU	202	30.258	4.996	28.014	1.00	17.08
ATOM	1581	CB	LEU	202	29.805	5.866	29.195	1.00	15.75
ATOM	1582	CG	LEU	202	29.018	7.136	28.828	1.00	15.95
ATOM	1583	CD1	LEU	202	28.622	7.901	30.095	1.00	12.72
ATOM	1584	CD2	LEU	202	29.870	8.009	27.910	1.00	16.64
ATOM	1585	C	LEU	202	31.309	3.992	28.512	1.00	18.70
ATOM	1586	O	LEU	202	32.440	4.381	28.815	1.00	20.36
ATOM	1587	N	ALA	203	30.956	2.716	28.592	1.00	17.89
ATOM	1588	CA	ALA	203	31.906	1.721	29.088	1.00	19.09
ATOM	1589	CB	ALA	203	31.509	1.296	30.493	1.00	16.50
ATOM	1590	C	ALA	203	32.064	0.496	28.191	1.00	19.03
ATOM	1591	O	ALA	203	32.957	-0.334	28.404	1.00	19.86
ATOM	1592	N	GLY	204	31.197	0.373	27.195	1.00	17.84
ATOM	1593	CA	GLY	204	31.279	-0.756	26.283	1.00	19.26
ATOM	1594	C	GLY	204	30.967	-2.097	26.920	1.00	21.43
ATOM	1595	O	GLY	204	31.435	-3.137	26.453	1.00	23.21
ATOM	1596	N	GLU	205	30.199	-2.074	28.002	1.00	20.75

FIG.11A-38

ATOM	1597	CA	GLU	205	29.806	-3.302	28.688	1.00	20.39
ATOM	1598	CB	GLU	205	30.935	-3.826	29.588	1.00	22.16
ATOM	1599	CG	GLU	205	31.143	-3.074	30.887	1.00	27.49
ATOM	1600	CD	GLU	205	32.247	-3.681	31.751	1.00	29.22
ATOM	1601	OE1	GLU	205	32.138	-4.860	32.146	1.00	35.45
ATOM	1602	OE2	GLU	205	33.225	-2.971	32.040	1.00	28.80
ATOM	1603	C	GLU	205	28.563	-3.054	29.518	1.00	18.62
ATOM	1604	O	GLU	205	28.305	-1.932	29.958	1.00	19.35
ATOM	1605	N	LEU	206	27.779	-4.105	29.714	1.00	19.99
ATOM	1606	CA	LEU	206	26.562	-4.013	30.505	1.00	20.37
ATOM	1607	CB	LEU	206	25.543	-5.044	30.013	1.00	18.33
ATOM	1608	CG	LEU	206	24.899	-4.783	28.643	1.00	20.09
ATOM	1609	CD1	LEU	206	25.952	-4.511	27.586	1.00	30.30
ATOM	1610	CD2	LEU	206	24.075	-5.987	28.246	1.00	18.48
ATOM	1611	C	LEU	206	26.976	-4.290	31.944	1.00	21.02
ATOM	1612	O	LEU	206	27.769	-5.195	32.205	1.00	21.65
ATOM	1613	N	PRO	207	26.449	-3.510	32.898	1.00	21.06
ATOM	1614	CD	PRO	207	25.507	-2.400	32.678	1.00	18.20
ATOM	1615	CA	PRO	207	26.760	-3.646	34.323	1.00	21.75
ATOM	1616	CB	PRO	207	26.118	-2.405	34.932	1.00	19.82
ATOM	1617	CG	PRO	207	24.920	-2.200	34.055	1.00	17.27
ATOM	1618	C	PRO	207	26.330	-4.929	35.027	1.00	23.19
ATOM	1619	O	PRO	207	27.002	-5.363	35.958	1.00	25.40
ATOM	1620	N	TRP	208	25.222	-5.533	34.600	1.00	20.85
ATOM	1621	CA	TRP	208	24.759	-6.768	35.227	1.00	19.87
ATOM	1622	CB	TRP	208	24.037	-6.449	36.542	1.00	17.82
ATOM	1623	CG	TRP	208	23.079	-5.294	36.431	1.00	16.93
ATOM	1624	CD2	TRP	208	23.259	-3.986	36.978	1.00	15.33
ATOM	1625	CE2	TRP	208	22.156	-3.203	36.564	1.00	19.36
ATOM	1626	CE3	TRP	208	24.245	-3.394	37.777	1.00	16.72
ATOM	1627	CD1	TRP	208	21.906	-5.261	35.730	1.00	19.54
ATOM	1628	NE1	TRP	208	21.344	-4.005	35.805	1.00	19.05
ATOM	1629	CZ2	TRP	208	22.017	-1.861	36.923	1.00	17.14
ATOM	1630	CZ3	TRP	208	24.102	-2.057	38.137	1.00	17.80
ATOM	1631	CH2	TRP	208	22.994	-1.306	37.708	1.00	17.63
ATOM	1632	C	TRP	208	23.847	-7.604	34.334	1.00	21.19
ATOM	1633	O	TRP	208	23.243	-7.094	33.389	1.00	21.45
ATOM	1634	N	ASP	209	23.758	-8.896	34.635	1.00	22.55
ATOM	1635	CA	ASP	209	22.901	-9.800	33.865	1.00	23.07
ATOM	1636	CB	ASP	209	23.087	-11.256	34.317	1.00	24.77
ATOM	1637	CG	ASP	209	24.456	-11.812	33.973	1.00	29.47
ATOM	1638	OD1	ASP	209	24.996	-11.464	32.901	1.00	32.08

FIG.11A-39

ATOM	1639	OD2	ASP	209	24.981	-12.619	34.770	1.00	37.34
ATOM	1640	C	ASP	209	21.439	-9.398	34.063	1.00	22.59
ATOM	1641	O	ASP	209	20.623	-9.498	33.143	1.00	21.49
ATOM	1642	N	GLN	210	21.123	-8.953	35.276	1.00	21.47
ATOM	1643	CA	GLN	210	19.775	-8.522	35.635	1.00	21.65
ATOM	1644	CB	GLN	210	18.832	-9.729	35.725	1.00	21.36
ATOM	1645	CG	GLN	210	19.346	-10.845	36.622	1.00	22.91
ATOM	1646	CD	GLN	210	18.428	-12.051	36.635	1.00	24.69
ATOM	1647	OE1	GLN	210	18.188	-12.676	35.600	1.00	28.77
ATOM	1648	NE2	GLN	210	17.905	-12.383	37.810	1.00	29.76
ATOM	1649	C	GLN	210	19.832	-7.792	36.972	1.00	24.10
ATOM	1650	O	GLN	210	20.731	-8.031	37.789	1.00	24.28
ATOM	1651	N	PRO	211	18.874	-6.886	37.214	1.00	23.45
ATOM	1652	CD	PRO	211	17.887	-6.387	36.234	1.00	19.42
ATOM	1653	CA	PRO	211	18.815	-6.108	38.451	1.00	23.88
ATOM	1654	CB	PRO	211	18.038	-4.869	38.024	1.00	23.48
ATOM	1655	CG	PRO	211	17.044	-5.443	37.072	1.00	18.80
ATOM	1656	C	PRO	211	18.169	-6.826	39.634	1.00	25.58
ATOM	1657	O	PRO	211	17.121	-6.407	40.127	1.00	25.13
ATOM	1658	N	SER	212	18.811	-7.898	40.091	1.00	27.11
ATOM	1659	CA	SER	212	18.303	-8.678	41.214	1.00	30.46
ATOM	1660	CB	SER	212	18.006	-10.110	40.770	1.00	30.00
ATOM	1661	OG	SER	212	17.174	-10.129	39.621	1.00	37.91
ATOM	1662	C	SER	212	19.324	-8.707	42.349	1.00	32.05
ATOM	1663	O	SER	212	20.524	-8.599	42.117	1.00	30.68
ATOM	1664	N	ASP	213	18.834	-8.857	43.575	1.00	35.30
ATOM	1665	CA	ASP	213	19.706	-8.912	44.741	1.00	39.23
ATOM	1666	CB	ASP	213	18.866	-9.031	46.014	1.00	46.49
ATOM	1667	CG	ASP	213	18.025	-7.795	46.273	1.00	52.63
ATOM	1668	OD1	ASP	213	17.193	-7.823	47.204	1.00	56.41
ATOM	1669	OD2	ASP	213	18.199	-6.793	45.547	1.00	59.76
ATOM	1670	C	ASP	213	20.663	-10.098	44.632	1.00	38.86
ATOM	1671	O	ASP	213	21.765	-10.070	45.180	1.00	41.19
ATOM	1672	N	SER	214	20.235	-11.133	43.914	1.00	37.29
ATOM	1673	CA	SER	214	21.047	-12.329	43.721	1.00	36.16
ATOM	1674	CB	SER	214	20.186	-13.463	43.157	1.00	39.69
ATOM	1675	OG	SER	214	19.604	-13.090	41.917	1.00	44.23
ATOM	1676	C	SER	214	22.214	-12.063	42.774	1.00	35.29
ATOM	1677	O	SER	214	23.187	-12.819	42.746	1.00	37.89
ATOM	1678	N	CYS	215	22.110	-10.991	41.994	1.00	33.00
ATOM	1679	CA	CYS	215	23.159	-10.632	41.045	1.00	31.71
ATOM	1680	CB	CYS	215	22.557	-9.851	39.871	1.00	33.69

FIG.11A-40

ATOM	1681	SG	CYS	215	23.706	-9.553	38.523	1.00	33.80
ATOM	1682	C	CYS	215	24.223	-9.792	41.749	1.00	30.56
ATOM	1683	O	CYS	215	23.976	-8.648	42.123	1.00	30.45
ATOM	1684	N	GLN	216	25.410	-10.369	41.918	1.00	30.39
ATOM	1685	CA	GLN	216	26.497	-9.687	42.602	1.00	27.76
ATOM	1686	CB	GLN	216	27.753	-10.569	42.621	1.00	28.61
ATOM	1687	CG	GLN	216	28.854	-10.012	43.510	1.00	32.96
ATOM	1688	CD	GLN	216	28.421	-9.895	44.963	1.00	42.47
ATOM	1689	OE1	GLN	216	28.866	-9.004	45.686	1.00	41.12
ATOM	1690	NE2	GLN	216	27.554	-10.803	45.398	1.00	48.90
ATOM	1691	C	GLN	216	26.838	-8.319	42.014	1.00	26.11
ATOM	1692	O	GLN	216	27.078	-7.375	42.759	1.00	23.93
ATOM	1693	N	GLU	217	26.861	-8.212	40.688	1.00	25.76
ATOM	1694	CA	GLU	217	27.176	-6.937	40.045	1.00	23.96
ATOM	1695	CB	GLU	217	27.213	-7.092	38.521	1.00	24.39
ATOM	1696	CG	GLU	217	28.404	-7.884	37.980	1.00	27.80
ATOM	1697	CD	GLU	217	28.416	-9.327	38.453	1.00	30.02
ATOM	1698	OE1	GLU	217	27.330	-9.944	38.514	1.00	26.98
ATOM	1699	OE2	GLU	217	29.515	-9.845	38.754	1.00	34.80
ATOM	1700	C	GLU	217	26.154	-5.868	40.432	1.00	22.37
ATOM	1701	O	GLU	217	26.507	-4.701	40.629	1.00	20.68
ATOM	1702	N	TYR	218	24.888	-6.261	40.547	1.00	22.07
ATOM	1703	CA	TYR	218	23.858	-5.303	40.927	1.00	22.82
ATOM	1704	CB	TYR	218	22.454	-5.858	40.664	1.00	24.84
ATOM	1705	CG	TYR	218	21.371	-4.831	40.920	1.00	26.40
ATOM	1706	CD1	TYR	218	21.373	-3.611	40.245	1.00	22.79
ATOM	1707	CE1	TYR	218	20.402	-2.644	40.496	1.00	21.41
ATOM	1708	CD2	TYR	218	20.363	-5.062	41.856	1.00	27.38
ATOM	1709	CE2	TYR	218	19.385	-4.101	42.114	1.00	24.51
ATOM	1710	CZ	TYR	218	19.413	-2.896	41.433	1.00	21.04
ATOM	1711	OH	TYR	218	18.469	-1.929	41.702	1.00	23.17
ATOM	1712	C	TYR	218	23.991	-4.917	42.397	1.00	22.65
ATOM	1713	O	TYR	218	23.811	-3.754	42.750	1.00	23.66
ATOM	1714	N	SER	219	24.302	-5.888	43.256	1.00	25.18
ATOM	1715	CA	SER	219	24.470	-5.600	44.681	1.00	24.31
ATOM	1716	CB	SER	219	24.737	-6.889	45.471	1.00	26.30
ATOM	1717	OG	SER	219	23.648	-7.782	45.364	1.00	36.64
ATOM	1718	C	SER	219	25.629	-4.628	44.888	1.00	22.69
ATOM	1719	O	SER	219	25.527	-3.697	45.688	1.00	22.21
ATOM	1720	N	ASP	220	26.725	-4.853	44.168	1.00	24.43
ATOM	1721	CA	ASP	220	27.904	-3.992	44.257	1.00	24.43
ATOM	1722	CB	ASP	220	28.990	-4.469	43.288	1.00	23.90

FIG.11A-41

ATOM	1723	CG	ASP	220	29.662	-5.759	43.742	1.00	29.00
ATOM	1724	OD1	ASP	220	30.451	-6.320	42.954	1.00	35.56
ATOM	1725	OD2	ASP	220	29.406	-6.205	44.881	1.00	33.13
ATOM	1726	C	ASP	220	27.532	-2.545	43.935	1.00	24.18
ATOM	1727	O	ASP	220	28.007	-1.613	44.584	1.00	23.82
ATOM	1728	N	TRP	221	26.679	-2.360	42.930	1.00	22.56
ATOM	1729	CA	TRP	221	26.247	-1.016	42.545	1.00	20.51
ATOM	1730	CB	TRP	221	25.414	-1.090	41.256	1.00	19.85
ATOM	1731	CG	TRP	221	24.672	0.179	40.909	1.00	20.17
ATOM	1732	CD2	TRP	221	25.238	1.408	40.434	1.00	20.07
ATOM	1733	CE2	TRP	221	24.163	2.309	40.226	1.00	17.90
ATOM	1734	CE3	TRP	221	26.542	1.841	40.165	1.00	17.56
ATOM	1735	CD1	TRP	221	23.322	0.378	40.972	1.00	18.44
ATOM	1736	NE1	TRP	221	23.008	1.653	40.563	1.00	18.49
ATOM	1737	CZ2	TRP	221	24.360	3.614	39.758	1.00	15.58
ATOM	1738	CZ3	TRP	221	26.738	3.141	39.701	1.00	18.36
ATOM	1739	CH2	TRP	221	25.650	4.012	39.501	1.00	17.00
ATOM	1740	C	TRP	221	25.446	-0.356	43.667	1.00	21.95
ATOM	1741	O	TRP	221	25.662	0.810	43.995	1.00	21.87
ATOM	1742	N	LYS	222	24.521	-1.099	44.262	1.00	24.52
ATOM	1743	CA	LYS	222	23.721	-0.543	45.343	1.00	26.38
ATOM	1744	CB	LYS	222	22.596	-1.505	45.726	1.00	27.07
ATOM	1745	CG	LYS	222	21.565	-1.698	44.618	1.00	24.09
ATOM	1746	CD	LYS	222	20.299	-2.376	45.123	1.00	27.22
ATOM	1747	CE	LYS	222	20.538	-3.831	45.493	1.00	25.58
ATOM	1748	NZ	LYS	222	19.279	-4.473	45.958	1.00	28.43
ATOM	1749	C	LYS	222	24.601	-0.233	46.553	1.00	28.55
ATOM	1750	O	LYS	222	24.251	0.601	47.385	1.00	29.05
ATOM	1751	N	GLU	223	25.750	-0.898	46.635	1.00	29.11
ATOM	1752	CA	GLU	223	26.691	-0.674	47.730	1.00	31.70
ATOM	1753	CB	GLU	223	27.482	-1.950	48.026	1.00	35.51
ATOM	1754	CG	GLU	223	26.650	-3.085	48.592	1.00	49.01
ATOM	1755	CD	GLU	223	27.485	-4.311	48.900	1.00	57.47
ATOM	1756	OE1	GLU	223	28.415	-4.205	49.726	1.00	62.72
ATOM	1757	OE2	GLU	223	27.214	-5.381	48.313	1.00	63.79
ATOM	1758	C	GLU	223	27.658	0.455	47.381	1.00	32.76
ATOM	1759	O	GLU	223	28.578	0.756	48.144	1.00	33.37
ATOM	1760	N	LYS	224	27.446	1.068	46.219	1.00	32.14
ATOM	1761	CA	LYS	224	28.272	2.178	45.745	1.00	33.92
ATOM	1762	CB	LYS	224	28.229	3.338	46.750	1.00	38.46
ATOM	1763	CG	LYS	224	26.913	4.109	46.777	1.00	46.23
ATOM	1764	CD	LYS	224	25.775	3.286	47.359	1.00	56.20

FIG.11A-42

ATOM	1765	CE	LYS	224	25.974	3.040	48.848	1.00	61.78
ATOM	1766	NZ	LYS	224	25.995	4.315	49.618	1.00	65.83
ATOM	1767	C	LYS	224	29.729	1.830	45.440	1.00	34.18
ATOM	1768	O	LYS	224	30.615	2.673	45.573	1.00	34.19
ATOM	1769	N	LYS	225	29.978	0.597	45.016	1.00	33.64
ATOM	1770	CA	LYS	225	31.336	0.172	44.688	1.00	35.23
ATOM	1771	CB	LYS	225	31.453	-1.347	44.837	1.00	36.69
ATOM	1772	CG	LYS	225	31.093	-1.853	46.230	1.00	40.35
ATOM	1773	CD	LYS	225	31.044	-3.377	46.290	1.00	46.38
ATOM	1774	CE	LYS	225	32.383	-4.004	45.943	1.00	52.69
ATOM	1775	NZ	LYS	225	32.346	-5.490	46.067	1.00	60.52
ATOM	1776	C	LYS	225	31.670	0.588	43.254	1.00	36.02
ATOM	1777	O	LYS	225	31.918	-0.255	42.391	1.00	34.27
ATOM	1778	N	THR	226	31.684	1.895	43.010	1.00	37.19
ATOM	1779	CA	THR	226	31.957	2.424	41.678	1.00	38.34
ATOM	1780	CB	THR	226	31.516	3.902	41.571	1.00	38.25
ATOM	1781	OG1	THR	226	32.145	4.670	42.602	1.00	38.16
ATOM	1782	CG2	THR	226	30.005	4.011	41.714	1.00	32.35
ATOM	1783	C	THR	226	33.409	2.303	41.227	1.00	39.24
ATOM	1784	O	THR	226	33.757	2.710	40.118	1.00	38.72
ATOM	1785	N	TYR	227	34.257	1.745	42.084	1.00	40.18
ATOM	1786	CA	TYR	227	35.658	1.560	41.733	1.00	39.40
ATOM	1787	CB	TYR	227	36.521	1.474	42.998	1.00	40.25
ATOM	1788	CG	TYR	227	36.050	0.445	43.999	1.00	41.05
ATOM	1789	CD1	TYR	227	36.283	-0.916	43.797	1.00	41.13
ATOM	1790	CE1	TYR	227	35.832	-1.867	44.709	1.00	37.13
ATOM	1791	CD2	TYR	227	35.353	0.831	45.143	1.00	38.67
ATOM	1792	CE2	TYR	227	34.897	-0.111	46.060	1.00	39.51
ATOM	1793	CZ	TYR	227	35.140	-1.456	45.837	1.00	39.20
ATOM	1794	OH	TYR	227	34.680	-2.387	46.738	1.00	46.31
ATOM	1795	C	TYR	227	35.776	0.280	40.914	1.00	39.74
ATOM	1796	O	TYR	227	36.862	-0.083	40.459	1.00	40.52
ATOM	1797	N	LEU	228	34.643	-0.395	40.728	1.00	39.05
ATOM	1798	CA	LEU	228	34.590	-1.634	39.962	1.00	39.33
ATOM	1799	CB	LEU	228	33.447	-2.523	40.456	1.00	40.20
ATOM	1800	CG	LEU	228	33.661	-3.195	41.817	1.00	45.84
ATOM	1801	CD1	LEU	228	32.410	-3.961	42.217	1.00	43.62
ATOM	1802	CD2	LEU	228	34.859	-4.135	41.740	1.00	44.55
ATOM	1803	C	LEU	228	34.442	-1.390	38.462	1.00	39.82
ATOM	1804	O	LEU	228	33.843	-0.403	38.033	1.00	37.15
ATOM	1805	N	ASN	229	34.987	-2.332	37.698	1.00	41.12
ATOM	1806	CA	ASN	229	35.041	-2.348	36.235	1.00	42.82

FIG.11A-43

ATOM	1807	CB	ASN	229	34.836	-3.784	35.733	1.00	47.56
ATOM	1808	CG	ASN	229	35.542	-4.046	34.413	1.00	53.15
ATOM	1809	OD1	ASN	229	36.739	-3.789	34.276	1.00	50.92
ATOM	1810	ND2	ASN	229	34.806	-4.567	33.438	1.00	57.87
ATOM	1811	C	ASN	229	34.192	-1.399	35.389	1.00	41.75
ATOM	1812	O	ASN	229	34.726	-0.466	34.785	1.00	44.90
ATOM	1813	N	PRO	230	32.866	-1.608	35.328	1.00	37.73
ATOM	1814	CD	PRO	230	31.965	-2.470	36.114	1.00	33.11
ATOM	1815	CA	PRO	230	32.103	-0.675	34.490	1.00	30.88
ATOM	1816	CB	PRO	230	30.680	-1.229	34.575	1.00	30.85
ATOM	1817	CG	PRO	230	30.624	-1.763	35.958	1.00	30.64
ATOM	1818	C	PRO	230	32.193	0.798	34.890	1.00	25.71
ATOM	1819	O	PRO	230	32.654	1.638	34.112	1.00	24.73
ATOM	1820	N	TRP	231	31.782	1.097	36.116	1.00	23.16
ATOM	1821	CA	TRP	231	31.757	2.462	36.635	1.00	21.32
ATOM	1822	CB	TRP	231	31.099	2.450	38.020	1.00	19.67
ATOM	1823	CG	TRP	231	29.965	1.469	38.087	1.00	23.28
ATOM	1824	CD2	TRP	231	28.741	1.522	37.344	1.00	21.23
ATOM	1825	CE2	TRP	231	28.023	0.344	37.637	1.00	20.01
ATOM	1826	CE3	TRP	231	28.188	2.451	36.450	1.00	20.09
ATOM	1827	CD1	TRP	231	29.934	0.297	38.789	1.00	22.83
ATOM	1828	NE1	TRP	231	28.773	-0.386	38.523	1.00	21.22
ATOM	1829	CZ2	TRP	231	26.774	0.067	37.071	1.00	19.20
ATOM	1830	CZ3	TRP	231	26.945	2.176	35.886	1.00	24.61
ATOM	1831	CH2	TRP	231	26.255	0.990	36.200	1.00	21.84
ATOM	1832	C	TRP	231	33.098	3.210	36.685	1.00	22.69
ATOM	1833	O	TRP	231	33.138	4.425	36.503	1.00	20.98
ATOM	1834	N	LYS	232	34.199	2.507	36.921	1.00	23.86
ATOM	1835	CA	LYS	232	35.487	3.199	36.992	1.00	25.79
ATOM	1836	CB	LYS	232	36.560	2.276	37.586	1.00	24.84
ATOM	1837	CG	LYS	232	36.812	0.989	36.824	1.00	33.96
ATOM	1838	CD	LYS	232	37.851	0.136	37.560	1.00	39.70
ATOM	1839	CE	LYS	232	38.112	-1.185	36.856	1.00	44.39
ATOM	1840	NZ	LYS	232	39.067	-2.042	37.620	1.00	48.06
ATOM	1841	C	LYS	232	35.962	3.760	35.649	1.00	25.77
ATOM	1842	O	LYS	232	36.920	4.530	35.596	1.00	26.85
ATOM	1843	N	LYS	233	35.277	3.393	34.570	1.00	24.28
ATOM	1844	CA	LYS	233	35.638	3.852	33.228	1.00	21.58
ATOM	1845	CB	LYS	233	35.460	2.714	32.220	1.00	21.63
ATOM	1846	CG	LYS	233	36.298	1.481	32.489	1.00	21.89
ATOM	1847	CD	LYS	233	36.181	0.466	31.357	1.00	21.02
ATOM	1848	CE	LYS	233	34.839	-0.229	31.329	1.00	23.92

FIG.11A-44

ATOM	1849	NZ	LYS	233	34.817	-1.324	30.311	1.00	24.83
ATOM	1850	C	LYS	233	34.800	5.025	32.731	1.00	22.49
ATOM	1851	O	LYS	233	35.041	5.545	31.642	1.00	22.51
ATOM	1852	N	ILE	234	33.848	5.471	33.533	1.00	23.05
ATOM	1853	CA	ILE	234	32.933	6.504	33.062	1.00	23.85
ATOM	1854	CB	ILE	234	31.526	6.124	33.584	1.00	18.85
ATOM	1855	CG2	ILE	234	30.523	7.242	33.345	1.00	16.49
ATOM	1856	CG1	ILE	234	31.128	4.813	32.893	1.00	16.83
ATOM	1857	CD1	ILE	234	29.773	4.256	33.265	1.00	15.87
ATOM	1858	C	ILE	234	33.206	8.015	33.175	1.00	26.97
ATOM	1859	O	ILE	234	33.655	8.629	32.202	1.00	34.42
ATOM	1860	N	ASP	235	32.953	8.592	34.339	1.00	25.59
ATOM	1861	CA	ASP	235	33.136	10.025	34.646	1.00	24.80
ATOM	1862	CB	ASP	235	32.528	10.995	33.623	1.00	22.82
ATOM	1863	CG	ASP	235	33.342	12.289	33.509	1.00	29.58
ATOM	1864	OD1	ASP	235	33.015	13.294	34.187	1.00	28.74
ATOM	1865	OD2	ASP	235	34.341	12.292	32.758	1.00	24.88
ATOM	1866	C	ASP	235	32.512	10.282	35.990	1.00	22.84
ATOM	1867	O	ASP	235	31.766	9.448	36.503	1.00	19.57
ATOM	1868	N	SER	236	32.824	11.450	36.540	1.00	22.97
ATOM	1869	CA	SER	236	32.144	11.667	37.793	1.00	23.58
ATOM	1870	CB	SER	236	32.929	12.818	38.441	1.00	22.04
ATOM	1871	OG	SER	236	32.992	13.941	37.583	1.00	27.67
ATOM	1872	C	SER	236	30.991	12.390	37.096	1.00	21.73
ATOM	1873	O	SER	236	29.952	12.112	37.692	1.00	19.53
ATOM	1874	N	ALA	237	31.031	13.258	36.083	1.00	20.61
ATOM	1875	CA	ALA	237	29.816	13.944	35.639	1.00	19.05
ATOM	1876	CB	ALA	237	30.137	14.988	34.566	1.00	14.22
ATOM	1877	C	ALA	237	28.746	12.973	35.134	1.00	17.61
ATOM	1878	O	ALA	237	27.639	12.950	35.664	1.00	17.49
ATOM	1879	N	PRO	238	29.049	12.175	34.097	1.00	15.48
ATOM	1880	CD	PRO	238	30.217	12.121	33.199	1.00	15.00
ATOM	1881	CA	PRO	238	27.999	11.252	33.646	1.00	16.82
ATOM	1882	CB	PRO	238	28.572	10.670	32.347	1.00	13.41
ATOM	1883	CG	PRO	238	30.067	10.766	32.552	1.00	10.20
ATOM	1884	C	PRO	238	27.670	10.183	34.694	1.00	14.91
ATOM	1885	O	PRO	238	26.539	9.701	34.770	1.00	14.08
ATOM	1886	N	LEU	239	28.657	9.815	35.508	1.00	16.50
ATOM	1887	CA	LEU	239	28.434	8.819	36.554	1.00	17.72
ATOM	1888	CB	LEU	239	29.744	8.522	37.296	1.00	18.57
ATOM	1889	CG	LEU	239	30.096	7.069	37.643	1.00	22.40
ATOM	1890	CD1	LEU	239	31.090	7.086	38.795	1.00	23.81

FIG.11A-45

ATOM	1891	CD2	LEU	239	28.873	6.257	38.017	1.00	22.04
ATOM	1892	C	LEU	239	27.394	9.351	37.543	1.00	17.57
ATOM	1893	O	LEU	239	26.543	8.605	38.026	1.00	16.91
ATOM	1894	N	ALA	240	27.464	10.645	37.846	1.00	16.87
ATOM	1895	CA	ALA	240	26.508	11.254	38.766	1.00	17.94
ATOM	1896	CB	ALA	240	26.867	12.725	39.024	1.00	15.97
ATOM	1897	C	ALA	240	25.091	11.143	38.198	1.00	16.55
ATOM	1898	O	ALA	240	24.136	10.974	38.950	1.00	16.22
ATOM	1899	N	LEU	241	24.954	11.241	36.878	1.00	15.65
ATOM	1900	CA	LEU	241	23.627	11.111	36.264	1.00	15.31
ATOM	1901	CB	LEU	241	23.652	11.540	34.785	1.00	12.35
ATOM	1902	CG	LEU	241	22.354	11.270	33.991	1.00	13.16
ATOM	1903	CD1	LEU	241	21.170	11.991	34.606	1.00	14.35
ATOM	1904	CD2	LEU	241	22.535	11.720	32.557	1.00	12.21
ATOM	1905	C	LEU	241	23.175	9.655	36.384	1.00	16.01
ATOM	1906	O	LEU	241	22.025	9.377	36.739	1.00	15.78
ATOM	1907	N	LEU	242	24.076	8.719	36.095	1.00	15.89
ATOM	1908	CA	LEU	242	23.734	7.303	36.194	1.00	16.35
ATOM	1909	CB	LEU	242	24.942	6.430	35.808	1.00	17.35
ATOM	1910	CG	LEU	242	25.054	5.624	34.500	1.00	22.28
ATOM	1911	CD1	LEU	242	23.930	5.888	33.505	1.00	16.11
ATOM	1912	CD2	LEU	242	26.412	5.912	33.896	1.00	15.21
ATOM	1913	C	LEU	242	23.291	6.979	37.624	1.00	16.88
ATOM	1914	O	LEU	242	22.418	6.135	37.834	1.00	15.72
ATOM	1915	N	HIS	243	23.883	7.652	38.609	1.00	18.68
ATOM	1916	CA	HIS	243	23.507	7.417	40.004	1.00	17.89
ATOM	1917	CB	HIS	243	24.436	8.178	40.958	1.00	17.93
ATOM	1918	CG	HIS	243	25.587	7.362	41.458	1.00	27.59
ATOM	1919	CD2	HIS	243	25.622	6.251	42.232	1.00	27.35
ATOM	1920	ND1	HIS	243	26.900	7.673	41.176	1.00	30.65
ATOM	1921	CE1	HIS	243	27.695	6.790	41.755	1.00	31.26
ATOM	1922	NE2	HIS	243	26.944	5.917	42.402	1.00	27.77
ATOM	1923	C	HIS	243	22.069	7.855	40.265	1.00	17.20
ATOM	1924	O	HIS	243	21.425	7.366	41.189	1.00	17.65
ATOM	1925	N	LYS	244	21.577	8.792	39.460	1.00	17.08
ATOM	1926	CA	LYS	244	20.212	9.279	39.617	1.00	17.67
ATOM	1927	CB	LYS	244	20.137	10.751	39.212	1.00	15.78
ATOM	1928	CG	LYS	244	20.904	11.670	40.163	1.00	19.56
ATOM	1929	CD	LYS	244	20.750	13.143	39.815	1.00	19.62
ATOM	1930	CE	LYS	244	21.549	13.543	38.581	1.00	15.60
ATOM	1931	NZ	LYS	244	21.582	15.043	38.422	1.00	18.38
ATOM	1932	C	LYS	244	19.213	8.447	38.805	1.00	16.94

FIG.11A-46

ATOM	1933	O	LYS	244	18.044	8.339	39.170	1.00	16.00
ATOM	1934	N	ILE	245	19.681	7.849	37.713	1.00	15.92
ATOM	1935	CA	ILE	245	18.812	7.023	36.871	1.00	14.11
ATOM	1936	CB	ILE	245	19.338	6.955	35.404	1.00	12.65
ATOM	1937	CG2	ILE	245	18.465	5.982	34.573	1.00	14.27
ATOM	1938	CG1	ILE	245	19.307	8.352	34.776	1.00	11.69
ATOM	1939	CD1	ILE	245	19.923	8.441	33.379	1.00	17.04
ATOM	1940	C	ILE	245	18.684	5.586	37.387	1.00	13.68
ATOM	1941	O	ILE	245	17.583	5.041	37.481	1.00	15.46
ATOM	1942	N	LEU	246	19.809	4.963	37.724	1.00	14.19
ATOM	1943	CA	LEU	246	19.765	3.574	38.173	1.00	15.34
ATOM	1944	CB	LEU	246	21.062	2.865	37.776	1.00	13.75
ATOM	1945	CG	LEU	246	21.346	2.984	36.278	1.00	10.86
ATOM	1946	CD1	LEU	246	22.703	2.364	35.923	1.00	12.91
ATOM	1947	CD2	LEU	246	20.211	2.303	35.512	1.00	14.82
ATOM	1948	C	LEU	246	19.477	3.429	39.663	1.00	18.00
ATOM	1949	O	LEU	246	20.229	2.803	40.422	1.00	18.52
ATOM	1950	N	VAL	247	18.357	4.022	40.057	1.00	17.55
ATOM	1951	CA	VAL	247	17.881	4.000	41.433	1.00	16.51
ATOM	1952	CB	VAL	247	17.268	5.356	41.795	1.00	15.11
ATOM	1953	CG1	VAL	247	16.553	5.278	43.136	1.00	19.34
ATOM	1954	CG2	VAL	247	18.380	6.408	41.842	1.00	16.66
ATOM	1955	C	VAL	247	16.834	2.899	41.513	1.00	18.51
ATOM	1956	O	VAL	247	15.903	2.864	40.709	1.00	18.14
ATOM	1957	N	GLU	248	16.990	2.000	42.481	1.00	16.77
ATOM	1958	CA	GLU	248	16.078	0.864	42.613	1.00	17.92
ATOM	1959	CB	GLU	248	16.522	-0.034	43.767	1.00	19.95
ATOM	1960	CG	GLU	248	15.805	-1.376	43.799	1.00	28.58
ATOM	1961	CD	GLU	248	16.404	-2.315	44.822	1.00	43.56
ATOM	1962	OE1	GLU	248	16.396	-1.965	46.021	1.00	48.24
ATOM	1963	OE2	GLU	248	16.889	-3.396	44.425	1.00	46.86
ATOM	1964	C	GLU	248	14.605	1.224	42.781	1.00	18.01
ATOM	1965	O	GLU	248	13.741	0.633	42.131	1.00	17.60
ATOM	1966	N	ASN	249	14.317	2.185	43.652	1.00	17.72
ATOM	1967	CA	ASN	249	12.940	2.611	43.886	1.00	16.89
ATOM	1968	CB	ASN	249	12.866	3.392	45.206	1.00	19.13
ATOM	1969	CG	ASN	249	11.480	3.970	45.480	1.00	21.33
ATOM	1970	OD1	ASN	249	10.562	3.832	44.676	1.00	21.93
ATOM	1971	ND2	ASN	249	11.331	4.624	46.631	1.00	17.12
ATOM	1972	C	ASN	249	12.480	3.483	42.716	1.00	15.11
ATOM	1973	O	ASN	249	12.954	4.607	42.553	1.00	16.33
ATOM	1974	N	PRO	250	11.550	2.978	41.880	1.00	15.15

FIG.11A-47

ATOM	1975	CD	PRO	250	10.830	1.694	41.960	1.00	16.54
ATOM	1976	CA	PRO	250	11.080	3.774	40.737	1.00	15.50
ATOM	1977	CB	PRO	250	10.110	2.825	40.025	1.00	14.37
ATOM	1978	CG	PRO	250	9.569	1.973	41.153	1.00	13.99
ATOM	1979	C	PRO	250	10.437	5.111	41.105	1.00	16.72
ATOM	1980	O	PRO	250	10.409	6.039	40.298	1.00	16.34
ATOM	1981	N	SER	251	9.910	5.211	42.321	1.00	17.93
ATOM	1982	CA	SER	251	9.296	6.460	42.744	1.00	18.37
ATOM	1983	CB	SER	251	8.391	6.212	43.954	1.00	18.23
ATOM	1984	OG	SER	251	7.326	5.351	43.584	1.00	20.47
ATOM	1985	C	SER	251	10.347	7.524	43.060	1.00	18.31
ATOM	1986	O	SER	251	10.075	8.720	42.944	1.00	21.19
ATOM	1987	N	ALA	252	11.549	7.092	43.430	1.00	17.56
ATOM	1988	CA	ALA	252	12.638	8.020	43.749	1.00	16.14
ATOM	1989	CB	ALA	252	13.471	7.479	44.919	1.00	17.50
ATOM	1990	C	ALA	252	13.545	8.257	42.544	1.00	16.13
ATOM	1991	O	ALA	252	14.355	9.184	42.533	1.00	18.76
ATOM	1992	N	ARG	253	13.408	7.410	41.530	1.00	16.12
ATOM	1993	CA	ARG	253	14.227	7.520	40.322	1.00	16.16
ATOM	1994	CB	ARG	253	13.888	6.363	39.382	1.00	15.22
ATOM	1995	CG	ARG	253	14.795	6.205	38.149	1.00	14.94
ATOM	1996	CD	ARG	253	14.429	4.904	37.433	1.00	14.49
ATOM	1997	NE	ARG	253	14.393	3.796	38.391	1.00	15.13
ATOM	1998	CZ	ARG	253	13.637	2.709	38.264	1.00	12.50
ATOM	1999	NH1	ARG	253	13.671	1.770	39.199	1.00	10.88
ATOM	2000	NH2	ARG	253	12.849	2.560	37.203	1.00	13.34
ATOM	2001	C	ARG	253	13.998	8.859	39.625	1.00	17.48
ATOM	2002	O	ARG	253	12.889	9.389	39.624	1.00	16.77
ATOM	2003	N	ILE	254	15.054	9.405	39.033	1.00	15.92
ATOM	2004	CA	ILE	254	14.952	10.684	38.346	1.00	14.89
ATOM	2005	CB	ILE	254	16.359	11.151	37.864	1.00	16.24
ATOM	2006	CG2	ILE	254	16.867	10.225	36.749	1.00	14.32
ATOM	2007	CG1	ILE	254	16.305	12.604	37.390	1.00	16.57
ATOM	2008	CD1	ILE	254	17.679	13.194	37.079	1.00	15.04
ATOM	2009	C	ILE	254	13.981	10.583	37.164	1.00	16.39
ATOM	2010	O	ILE	254	13.878	9.537	36.519	1.00	17.01
ATOM	2011	N	THR	255	13.242	11.660	36.908	1.00	17.02
ATOM	2012	CA	THR	255	12.292	11.692	35.800	1.00	16.23
ATOM	2013	CB	THR	255	11.037	12.517	36.147	1.00	16.45
ATOM	2014	OG1	THR	255	11.433	13.837	36.542	1.00	19.30
ATOM	2015	CG2	THR	255	10.263	11.864	37.276	1.00	16.34
ATOM	2016	C	THR	255	12.997	12.370	34.635	1.00	17.07

FIG.11A-48

ATOM	2017	O	THR	255	14.058	12.959	34.808	1.00	16.74
ATOM	2018	N	ILE	256	12.410	12.321	33.450	1.00	18.82
ATOM	2019	CA	ILE	256	13.070	12.954	32.320	1.00	18.31
ATOM	2020	CB	ILE	256	12.393	12.576	30.995	1.00	16.73
ATOM	2021	CG2	ILE	256	13.076	13.305	29.844	1.00	16.91
ATOM	2022	CG1	ILE	256	12.482	11.058	30.805	1.00	15.14
ATOM	2023	CD1	ILE	256	11.814	10.538	29.555	1.00	17.21
ATOM	2024	C	ILE	256	13.162	14.472	32.461	1.00	18.90
ATOM	2025	O	ILE	256	14.182	15.062	32.112	1.00	19.82
ATOM	2026	N	PRO	257	12.099	15.135	32.959	1.00	19.76
ATOM	2027	CD	PRO	257	10.697	14.733	33.185	1.00	18.99
ATOM	2028	CA	PRO	257	12.256	16.590	33.079	1.00	19.66
ATOM	2029	CB	PRO	257	10.948	17.019	33.739	1.00	19.59
ATOM	2030	CG	PRO	257	9.953	16.075	33.104	1.00	19.54
ATOM	2031	C	PRO	257	13.494	16.949	33.911	1.00	19.08
ATOM	2032	O	PRO	257	14.176	17.941	33.637	1.00	19.37
ATOM	2033	N	ASP	258	13.794	16.133	34.917	1.00	19.06
ATOM	2034	CA	ASP	258	14.958	16.373	35.760	1.00	18.81
ATOM	2035	CB	ASP	258	14.735	15.728	37.128	1.00	18.17
ATOM	2036	CG	ASP	258	13.772	16.542	37.978	1.00	23.21
ATOM	2037	OD1	ASP	258	13.193	16.012	38.948	1.00	23.28
ATOM	2038	OD2	ASP	258	13.611	17.738	37.652	1.00	23.96
ATOM	2039	C	ASP	258	16.266	15.922	35.101	1.00	18.56
ATOM	2040	O	ASP	258	17.327	16.504	35.349	1.00	20.13
ATOM	2041	N	ILE	259	16.197	14.906	34.246	1.00	18.38
ATOM	2042	CA	ILE	259	17.392	14.471	33.531	1.00	19.58
ATOM	2043	CB	ILE	259	17.114	13.239	32.618	1.00	16.93
ATOM	2044	CG2	ILE	259	18.241	13.063	31.600	1.00	14.51
ATOM	2045	CG1	ILE	259	16.994	11.966	33.464	1.00	16.72
ATOM	2046	CD1	ILE	259	16.489	10.748	32.677	1.00	11.48
ATOM	2047	C	ILE	259	17.823	15.659	32.659	1.00	21.42
ATOM	2048	O	ILE	259	19.005	15.958	32.543	1.00	20.64
ATOM	2049	N	LYS	260	16.851	16.354	32.070	1.00	23.12
ATOM	2050	CA	LYS	260	17.152	17.499	31.208	1.00	23.95
ATOM	2051	CB	LYS	260	15.876	18.020	30.538	1.00	25.83
ATOM	2052	CG	LYS	260	15.150	19.064	31.356	1.00	38.93
ATOM	2053	CD	LYS	260	13.885	19.551	30.678	1.00	48.71
ATOM	2054	CE	LYS	260	13.278	20.709	31.455	1.00	44.94
ATOM	2055	NZ	LYS	260	14.210	21.872	31.510	1.00	42.57
ATOM	2056	C	LYS	260	17.827	18.646	31.961	1.00	22.24
ATOM	2057	O	LYS	260	18.369	19.558	31.340	1.00	22.70
ATOM	2058	N	LYS	261	17.787	18.598	33.290	1.00	20.88

FIG.11A-49

ATOM	2059	CA	LYS	261	18.402	19.628	34.129	1.00	21.74
ATOM	2060	CB	LYS	261	17.474	19.984	35.298	1.00	24.31
ATOM	2061	CG	LYS	261	16.176	20.661	34.881	1.00	33.19
ATOM	2062	CD	LYS	261	15.245	20.857	36.071	1.00	47.75
ATOM	2063	CE	LYS	261	14.008	21.650	35.680	1.00	57.96
ATOM	2064	NZ	LYS	261	13.280	21.031	34.537	1.00	64.19
ATOM	2065	C	LYS	261	19.750	19.181	34.687	1.00	21.66
ATOM	2066	O	LYS	261	20.462	19.964	35.320	1.00	23.16
ATOM	2067	N	ASP	262	20.105	17.926	34.442	1.00	19.55
ATOM	2068	CA	ASP	262	21.352	17.371	34.950	1.00	19.62
ATOM	2069	CB	ASP	262	21.419	15.874	34.618	1.00	18.71
ATOM	2070	CG	ASP	262	22.781	15.266	34.903	1.00	15.55
ATOM	2071	OD1	ASP	262	23.584	15.162	33.955	1.00	14.99
ATOM	2072	OD2	ASP	262	23.049	14.889	36.064	1.00	15.43
ATOM	2073	C	ASP	262	22.588	18.102	34.437	1.00	19.73
ATOM	2074	O	ASP	262	22.628	18.557	33.294	1.00	20.79
ATOM	2075	N	ARG	263	23.600	18.209	35.290	1.00	18.70
ATOM	2076	CA	ARG	263	24.825	18.910	34.925	1.00	18.98
ATOM	2077	CB	ARG	263	25.798	18.937	36.109	1.00	20.52
ATOM	2078	CG	ARG	263	27.078	19.713	35.820	1.00	28.61
ATOM	2079	CD	ARG	263	27.963	19.850	37.068	1.00	38.40
ATOM	2080	NE	ARG	263	28.937	18.768	37.219	1.00	45.20
ATOM	2081	CZ	ARG	263	28.637	17.502	37.499	1.00	56.82
ATOM	2082	NH1	ARG	263	27.375	17.129	37.665	1.00	58.45
ATOM	2083	NH2	ARG	263	29.607	16.606	37.626	1.00	62.85
ATOM	2084	C	ARG	263	25.516	18.320	33.700	1.00	18.37
ATOM	2085	O	ARG	263	25.850	19.046	32.769	1.00	17.68
ATOM	2086	N	TRP	264	25.732	17.008	33.684	1.00	17.26
ATOM	2087	CA	TRP	264	26.390	16.400	32.531	1.00	15.96
ATOM	2088	CB	TRP	264	26.684	14.918	32.788	1.00	15.01
ATOM	2089	CG	TRP	264	27.354	14.260	31.610	1.00	14.46
ATOM	2090	CD2	TRP	264	26.733	13.407	30.639	1.00	16.57
ATOM	2091	CE2	TRP	264	27.715	13.090	29.672	1.00	14.53
ATOM	2092	CE3	TRP	264	25.437	12.878	30.490	1.00	15.64
ATOM	2093	CD1	TRP	264	28.652	14.419	31.205	1.00	12.93
ATOM	2094	NE1	TRP	264	28.875	13.722	30.042	1.00	13.60
ATOM	2095	CZ2	TRP	264	27.446	12.269	28.570	1.00	14.44
ATOM	2096	CZ3	TRP	264	25.168	12.061	29.391	1.00	13.46
ATOM	2097	CH2	TRP	264	26.166	11.764	28.447	1.00	13.11
ATOM	2098	C	TRP	264	25.545	16.540	31.260	1.00	15.93
ATOM	2099	O	TRP	264	26.064	16.818	30.179	1.00	13.92
ATOM	2100	N	TYR	265	24.240	16.339	31.393	1.00	15.00

FIG.11A-50

ATOM	2101	CA	TYR	265	23.342	16.447	30.257	1.00	13.62
ATOM	2102	CB	TYR	265	21.895	16.265	30.738	1.00	11.92
ATOM	2103	CG	TYR	265	20.888	16.112	29.629	1.00	15.19
ATOM	2104	CD1	TYR	265	20.259	17.220	29.060	1.00	16.33
ATOM	2105	CE1	TYR	265	19.317	17.062	28.039	1.00	16.52
ATOM	2106	CD2	TYR	265	20.555	14.843	29.150	1.00	13.45
ATOM	2107	CE2	TYR	265	19.628	14.676	28.148	1.00	13.56
ATOM	2108	CZ	TYR	265	19.010	15.781	27.594	1.00	16.67
ATOM	2109	OH	TYR	265	18.084	15.582	26.608	1.00	19.16
ATOM	2110	C	TYR	265	23.508	17.798	29.551	1.00	14.32
ATOM	2111	O	TYR	265	23.459	17.882	28.322	1.00	15.01
ATOM	2112	N	ASN	266	23.751	18.847	30.335	1.00	15.47
ATOM	2113	CA	ASN	266	23.897	20.193	29.790	1.00	17.01
ATOM	2114	CB	ASN	266	23.166	21.184	30.704	1.00	17.43
ATOM	2115	CG	ASN	266	21.661	21.021	30.636	1.00	19.60
ATOM	2116	OD1	ASN	266	21.030	21.428	29.659	1.00	21.30
ATOM	2117	ND2	ASN	266	21.080	20.396	31.661	1.00	19.15
ATOM	2118	C	ASN	266	25.330	20.676	29.552	1.00	18.03
ATOM	2119	O	ASN	266	25.536	21.820	29.154	1.00	16.54
ATOM	2120	N	LYS	267	26.319	19.815	29.773	1.00	18.76
ATOM	2121	CA	LYS	267	27.716	20.221	29.574	1.00	18.99
ATOM	2122	CB	LYS	267	28.666	19.244	30.273	1.00	24.39
ATOM	2123	CG	LYS	267	28.804	19.442	31.769	1.00	35.68
ATOM	2124	CD	LYS	267	29.767	18.424	32.368	1.00	48.27
ATOM	2125	CE	LYS	267	31.138	18.481	31.702	1.00	51.14
ATOM	2126	NZ	LYS	267	31.800	19.802	31.888	1.00	56.24
ATOM	2127	C	LYS	267	28.123	20.307	28.110	1.00	19.25
ATOM	2128	O	LYS	267	27.919	19.365	27.350	1.00	18.64
ATOM	2129	N	PRO	268	28.708	21.444	27.694	1.00	21.76
ATOM	2130	CD	PRO	268	28.826	22.742	28.378	1.00	22.13
ATOM	2131	CA	PRO	268	29.119	21.547	26.289	1.00	23.47
ATOM	2132	CB	PRO	268	29.556	23.008	26.158	1.00	22.99
ATOM	2133	CG	PRO	268	28.746	23.713	27.219	1.00	24.42
ATOM	2134	C	PRO	268	30.276	20.570	26.084	1.00	22.96
ATOM	2135	O	PRO	268	31.280	20.627	26.800	1.00	22.64
ATOM	2136	N	LEU	269	30.132	19.670	25.120	1.00	21.85
ATOM	2137	CA	LEU	269	31.155	18.667	24.863	1.00	23.57
ATOM	2138	CB	LEU	269	30.751	17.324	25.473	1.00	23.55
ATOM	2139	CG	LEU	269	30.576	17.187	26.982	1.00	22.37
ATOM	2140	CD1	LEU	269	29.980	15.818	27.298	1.00	23.62
ATOM	2141	CD2	LEU	269	31.920	17.367	27.665	1.00	21.81
ATOM	2142	C	LEU	269	31.442	18.424	23.394	1.00	26.56

FIG.11A-51

ATOM	2143	O	LEU	269	32.592	18.228	23.012	1.00	26.46
ATOM	2144	N	LYS	270	30.400	18.421	22.571	1.00	28.53
ATOM	2145	CA	LYS	270	30.595	18.128	21.158	1.00	31.73
ATOM	2146	CB	LYS	270	29.790	16.881	20.777	1.00	33.10
ATOM	2147	CG	LYS	270	30.179	16.292	19.431	1.00	37.08
ATOM	2148	CD	LYS	270	29.461	14.981	19.167	1.00	35.35
ATOM	2149	CE	LYS	270	29.881	14.383	17.833	1.00	33.40
ATOM	2150	NZ	LYS	270	29.137	13.123	17.546	1.00	40.91
ATOM	2151	C	LYS	270	30.290	19.241	20.171	1.00	34.07
ATOM	2152	O	LYS	270	29.304	19.968	20.301	1.00	34.39
ATOM	2153	N	LYS	271	31.162	19.358	19.177	1.00	36.37
ATOM	2154	CA	LYS	271	31.018	20.349	18.124	1.00	39.68
ATOM	2155	CB	LYS	271	32.345	20.528	17.381	1.00	40.41
ATOM	2156	CG	LYS	271	33.534	20.899	18.259	1.00	37.20
ATOM	2157	CD	LYS	271	33.431	22.328	18.752	1.00	32.85
ATOM	2158	CE	LYS	271	34.718	22.773	19.440	1.00	26.35
ATOM	2159	NZ	LYS	271	34.639	24.202	19.855	1.00	21.18
ATOM	2160	C	LYS	271	29.975	19.818	17.146	1.00	41.40
ATOM	2161	O	LYS	271	29.709	18.615	17.109	1.00	39.59
ATOM	2162	N	GLY	272	29.393	20.711	16.354	1.00	43.87
ATOM	2163	CA	GLY	272	28.407	20.287	15.377	1.00	46.49
ATOM	2164	C	GLY	272	29.090	19.497	14.275	1.00	49.32
ATOM	2165	O	GLY	272	30.317	19.377	14.269	1.00	49.55
ATOM	2166	N	ALA	273	28.306	18.958	13.346	1.00	50.80
ATOM	2167	CA	ALA	273	28.850	18.175	12.240	1.00	53.37
ATOM	2168	CB	ALA	273	27.749	17.859	11.234	1.00	52.51
ATOM	2169	C	ALA	273	29.998	18.905	11.547	1.00	55.13
ATOM	2170	O	ALA	273	30.024	20.134	11.501	1.00	55.65
ATOM	2171	N	ALA	274	30.945	18.140	11.012	1.00	56.46
ATOM	2172	CA	ALA	274	32.101	18.707	10.323	1.00	57.69
ATOM	2173	CB	ALA	274	33.043	17.591	9.883	1.00	55.97
ATOM	2174	C	ALA	274	31.681	19.539	9.116	1.00	58.75
ATOM	2175	O	ALA	274	31.092	19.018	8.169	1.00	58.34
ATOM	2176	N	ALA	275	31.991	20.833	9.157	1.00	60.19
ATOM	2177	CA	ALA	275	31.653	21.751	8.073	1.00	61.34
ATOM	2178	CB	ALA	275	32.417	21.370	6.808	1.00	63.01
ATOM	2179	C	ALA	275	30.155	21.764	7.794	1.00	62.70
ATOM	2180	O	ALA	275	29.687	21.161	6.827	1.00	64.42
ATOM	2181	N	ALA	276	29.406	22.459	8.644	1.00	63.05
ATOM	2182	CA	ALA	276	27.959	22.553	8.493	1.00	64.39
ATOM	2183	CB	ALA	276	27.300	21.252	8.938	1.00	65.25
ATOM	2184	C	ALA	276	27.409	23.722	9.302	1.00	66.43

FIG.11A-52

ATOM	2185	OCT1	ALA	276	26.726	24.582	8.707	1.00	66.01
ATOM	2186	OT	ALA	276	27.665	23.761	10.524	1.00	72.06
ATOM	2187	OH2	WAT	500	7.288	0.582	30.446	1.00	12.93
ATOM	2188	OH2	WAT	501	7.551	-2.385	30.926	1.00	14.51
ATOM	2189	OH2	WAT	502	15.648	-3.549	26.581	1.00	12.66
ATOM	2190	OH2	WAT	503	22.995	-4.531	32.505	1.00	14.00
ATOM	2191	OH2	WAT	504	12.370	-2.139	29.668	1.00	12.75
ATOM	2192	OH2	WAT	505	8.243	1.795	37.412	1.00	13.95
ATOM	2193	OH2	WAT	506	12.211	-1.687	42.460	1.00	18.17
ATOM	2194	OH2	WAT	507	12.547	0.038	27.856	1.00	14.35
ATOM	2195	OH2	WAT	508	9.787	10.899	33.147	1.00	15.08
ATOM	2196	OH2	WAT	510	11.744	7.842	36.365	1.00	15.19
ATOM	2197	OH2	WAT	511	9.925	-3.492	29.777	1.00	15.10
ATOM	2198	OH2	WAT	512	9.590	8.537	34.696	1.00	17.43
ATOM	2199	OH2	WAT	513	2.021	3.295	33.836	1.00	15.34
ATOM	2200	OH2	WAT	514	6.563	13.229	27.860	1.00	18.19
ATOM	2201	OH2	WAT	515	10.555	8.269	38.785	1.00	18.00
ATOM	2202	OH2	WAT	516	10.674	15.405	22.497	1.00	19.56
ATOM	2203	OH2	WAT	517	25.750	15.101	36.287	1.00	17.00
ATOM	2204	OH2	WAT	518	4.386	6.182	34.218	1.00	15.43
ATOM	2205	OH2	WAT	519	13.712	-1.171	31.851	1.00	19.69
ATOM	2206	OH2	WAT	520	27.652	18.967	23.808	1.00	20.13
ATOM	2207	OH2	WAT	521	14.113	-4.152	28.944	1.00	16.61
ATOM	2208	OH2	WAT	522	8.101	9.135	38.813	1.00	23.68
ATOM	2209	OH2	WAT	523	6.549	1.866	39.438	1.00	17.99
ATOM	2210	OH2	WAT	524	8.387	10.486	30.847	1.00	15.91
ATOM	2211	OH2	WAT	525	12.082	9.839	11.918	1.00	19.48
ATOM	2212	OH2	WAT	526	18.804	-3.707	34.246	1.00	13.10
ATOM	2213	OH2	WAT	527	13.250	13.468	39.304	1.00	19.10
ATOM	2214	OH2	WAT	528	7.275	8.982	36.188	1.00	19.69
ATOM	2215	OH2	WAT	529	5.361	7.284	36.859	1.00	17.02
ATOM	2216	OH2	WAT	530	8.547	12.919	29.494	1.00	20.63
ATOM	2217	OH2	WAT	531	33.657	6.673	29.562	1.00	19.62
ATOM	2218	OH2	WAT	532	23.095	17.810	38.035	1.00	20.16
ATOM	2219	OH2	WAT	533	7.044	4.516	40.668	1.00	18.41
ATOM	2220	OH2	WAT	534	8.572	-2.181	21.497	1.00	19.99
ATOM	2221	OH2	WAT	535	5.165	-3.897	30.946	1.00	16.72
ATOM	2222	OH2	WAT	536	35.064	12.912	30.402	1.00	24.78
ATOM	2223	OH2	WAT	537	7.785	2.872	44.403	1.00	19.77
ATOM	2224	OH2	WAT	538	2.503	10.234	33.144	1.00	23.38
ATOM	2225	OH2	WAT	539	2.763	-3.299	20.083	1.00	22.50
ATOM	2226	OH2	WAT	540	6.475	6.912	39.440	1.00	22.13

FIG.11A-53

ATOM	2227	OH2	WAT	541	-6.228	9.593	24.818	1.00 26.15
ATOM	2228	OH2	WAT	542	37.153	5.154	30.029	1.00 23.86
ATOM	2229	OH2	WAT	543	8.552	2.510	13.829	1.00 21.71
ATOM	2230	OH2	WAT	544	16.101	3.059	45.670	1.00 22.52
ATOM	2231	OH2	WAT	545	32.130	14.940	31.845	1.00 22.82
ATOM	2232	OH2	WAT	546	18.050	14.095	15.782	1.00 22.03
ATOM	2233	OH2	WAT	547	24.287	11.877	41.531	1.00 25.65
ATOM	2234	OH2	WAT	548	0.491	-4.750	31.613	1.00 21.18
ATOM	2235	OH2	WAT	549	7.787	12.606	34.142	1.00 23.30
ATOM	2236	OH2	WAT	550	12.435	-5.647	20.701	1.00 31.34
ATOM	2237	OH2	WAT	552	25.857	-10.012	36.222	1.00 28.63
ATOM	2238	OH2	WAT	553	3.334	15.175	20.677	1.00 36.96
ATOM	2239	OH2	WAT	554	-4.014	0.643	36.230	1.00 24.61
ATOM	2240	OH2	WAT	555	10.571	-0.361	-16.930	1.00 26.27
ATOM	2241	OH2	WAT	556	14.828	-2.773	15.913	1.00 23.41
ATOM	2242	OH2	WAT	557	5.825	15.674	24.158	1.00 27.12
ATOM	2243	OH2	WAT	558	10.922	19.080	30.780	1.00 31.85
ATOM	2244	OH2	WAT	559	28.720	-6.638	28.476	1.00 27.77
ATOM	2245	OH2	WAT	560	3.832	-6.269	44.319	1.00 30.04
ATOM	2246	OH2	WAT	561	4.426	13.762	22.733	1.00 17.65
ATOM	2247	OH2	WAT	563	28.205	-3.067	39.437	1.00 24.33
ATOM	2248	OH2	WAT	564	2.857	8.453	37.278	1.00 24.76
ATOM	2249	OH2	WAT	565	25.621	21.668	32.817	1.00 22.51
ATOM	2250	OH2	WAT	566	10.036	-1.136	43.949	1.00 22.61
ATOM	2251	OH2	WAT	567	19.146	16.682	37.504	1.00 23.78
ATOM	2252	OH2	WAT	568	8.258	8.945	13.451	1.00 26.53
ATOM	2253	OH2	WAT	569	5.792	10.982	34.708	1.00 27.31
ATOM	2254	OH2	WAT	570	4.400	12.602	29.260	1.00 24.68
ATOM	2255	OH2	WAT	571	8.030	15.813	22.347	1.00 24.44
ATOM	2256	OH2	WAT	572	30.240	10.872	40.240	1.00 30.85
ATOM	2257	OH2	WAT	573	3.021	5.306	42.778	1.00 33.27
ATOM	2258	OH2	WAT	574	12.290	16.620	24.591	1.00 34.06
ATOM	2259	OH2	WAT	575	2.437	-4.157	42.875	1.00 24.07
ATOM	2260	OH2	WAT	576	19.000	2.392	44.605	1.00 32.41
ATOM	2261	OH2	WAT	577	-3.658	4.410	15.376	1.00 31.82
ATOM	2262	OH2	WAT	578	17.547	12.393	41.174	1.00 28.94
ATOM	2263	OH2	WAT	579	9.859	-9.730	26.441	1.00 24.36
ATOM	2264	OH2	WAT	580	7.649	-1.350	14.768	1.00 29.54
ATOM	2265	OH2	WAT	581	12.303	-0.250	12.412	1.00 26.66
ATOM	2266	OH2	WAT	582	6.958	15.256	16.519	1.00 46.73
ATOM	2267	OH2	WAT	583	4.897	12.398	31.727	1.00 29.49
ATOM	2268	OH2	WAT	584	17.449	-10.259	23.231	1.00 43.02

FIG.11A-54

ATOM	2269	OH2	WAT	585	-8.993	2.971	28.486	1.00 30.80
ATOM	2270	OH2	WAT	586	-0.139	-3.655	43.071	1.00 37.06
ATOM	2271	OH2	WAT	588	16.750	16.297	23.374	1.00 29.48
ATOM	2272	OH2	WAT	589	5.136	6.789	43.328	1.00 32.09
ATOM	2273	OH2	WAT	590	5.961	15.786	26.926	1.00 22.25
ATOM	2274	OH2	WAT	591	11.771	0.434	-14.604	1.00 25.03
ATOM	2275	OH2	WAT	592	20.674	-11.849	31.603	1.00 28.56
ATOM	2276	OH2	WAT	593	16.561	0.669	8.704	1.00 30.46
ATOM	2277	OH2	WAT	594	25.900	1.235	13.342	1.00 25.92
ATOM	2278	OH2	WAT	595	14.762	0.666	-11.939	1.00 27.07
ATOM	2279	OH2	WAT	596	19.928	0.579	42.222	1.00 33.09
ATOM	2280	OH2	WAT	597	2.749	-4.838	23.485	1.00 28.02
ATOM	2281	OH2	WAT	599	2.241	-12.981	17.063	1.00 32.27
ATOM	2282	OH2	WAT	600	17.311	-11.858	43.919	1.00 46.62
ATOM	2283	OH2	WAT	601	10.116	0.287	13.907	1.00 23.36
ATOM	2284	OH2	WAT	602	-5.766	4.131	31.307	1.00 37.38
ATOM	2285	OH2	WAT	603	8.777	-6.752	16.659	1.00 36.23
ATOM	2286	OH2	WAT	604	2.780	13.085	33.578	1.00 56.17
ATOM	2287	OH2	WAT	605	13.505	-9.621	24.772	1.00 27.48
ATOM	2288	OH2	WAT	606	19.499	-8.171	22.784	1.00 35.47
ATOM	2289	OH2	WAT	607	18.981	6.434	6.609	1.00 39.96
ATOM	2290	OH2	WAT	609	19.617	1.498	-10.274	1.00 46.75
ATOM	2291	OH2	WAT	610	7.105	14.231	31.956	1.00 30.92
ATOM	2292	OH2	WAT	611	-2.597	7.596	24.441	1.00 52.94
ATOM	2293	OH2	WAT	612	38.962	0.347	34.269	1.00 28.21
ATOM	2294	OH2	WAT	613	34.567	6.357	38.002	1.00 53.59
ATOM	2295	OH2	WAT	614	19.967	5.584	-11.241	1.00 30.33
ATOM	2296	OH2	WAT	615	0.984	14.444	27.279	1.00 41.31
ATOM	2297	OH2	WAT	616	31.944	18.357	34.770	1.00 56.14
ATOM	2298	OH2	WAT	617	23.842	3.527	43.838	1.00 39.09
ATOM	2299	OH2	WAT	618	24.265	-10.048	29.048	1.00 43.37
ATOM	2300	OH2	WAT	619	13.920	0.583	10.143	1.00 28.77
ATOM	2301	OH2	WAT	620	13.884	17.699	20.194	1.00 53.38
ATOM	2302	OH2	WAT	621	15.456	13.880	40.976	1.00 38.26
ATOM	2303	OH2	WAT	622	-4.209	10.695	27.546	1.00 31.65
ATOM	2304	OH2	WAT	623	9.422	15.446	37.303	1.00 35.02
ATOM	2305	OH2	WAT	624	28.277	9.830	16.219	1.00 32.83
ATOM	2306	OH2	WAT	625	-2.164	-0.376	23.957	1.00 32.44
ATOM	2307	OH2	WAT	626	13.795	-8.227	22.617	1.00 47.18
ATOM	2308	OH2	WAT	627	12.663	-2.391	45.836	1.00 32.05
ATOM	2309	OH2	WAT	628	3.919	-11.060	32.966	1.00 44.73
ATOM	2310	OH2	WAT	629	-2.517	11.533	34.098	1.00 54.44

FIG.11A-55

ATOM	2311	OH2	WAT	630	25.613	14.652	11.863	1.00 63.79
ATOM	2312	OH2	WAT	631	11.909	11.704	41.097	1.00 34.25
ATOM	2313	OH2	WAT	632	-1.360	10.995	26.456	1.00 38.16
ATOM	2314	OH2	WAT	633	31.933	5.045	17.791	1.00 39.91
ATOM	2315	OH2	WAT	634	22.722	-5.823	24.321	1.00 28.24
ATOM	2316	OH2	WAT	635	16.867	10.054	41.617	1.00 32.20
ATOM	2317	OH2	WAT	636	-0.030	10.808	17.607	1.00 37.23
ATOM	2318	OH2	WAT	637	-2.623	-2.811	32.773	1.00 41.25
ATOM	2319	OH2	WAT	638	31.929	21.354	29.330	1.00 38.21
ATOM	2320	OH2	WAT	639	17.980	15.951	20.755	1.00 60.27
ATOM	2321	OH2	WAT	640	29.018	-3.356	20.263	1.00 36.21
ATOM	2322	OH2	WAT	641	20.664	16.288	14.235	1.00 42.55
ATOM	2323	OH2	WAT	642	7.328	13.948	36.591	1.00 55.67
ATOM	2324	OH2	WAT	643	11.409	16.717	20.413	1.00 25.47
ATOM	2325	OH2	WAT	644	16.547	13.154	13.670	1.00 25.26
ATOM	2326	OH2	WAT	645	15.596	15.812	18.554	1.00 34.13
ATOM	2327	OH2	WAT	646	25.131	5.610	6.079	1.00 53.07
ATOM	2328	OH2	WAT	647	-3.556	15.275	34.402	1.00 61.62
ATOM	2329	OH2	WAT	648	10.229	-7.176	19.982	1.00 41.83
ATOM	2330	OH2	WAT	649	20.662	8.866	43.464	1.00 51.89
ATOM	2331	OH2	WAT	650	23.069	16.777	21.097	1.00 25.83
ATOM	2332	OH2	WAT	651	26.751	11.131	18.349	1.00 16.47
ATOM	2333	OH2	WAT	652	4.110	-8.428	37.000	1.00 23.09
ATOM	2334	OH2	WAT	654	16.700	-14.479	41.296	1.00 33.14
ATOM	2335	OH2	WAT	655	13.831	16.895	27.725	1.00 39.59
ATOM	2336	OH2	WAT	656	13.478	5.441	4.355	1.00 41.26
ATOM	2337	OH2	WAT	657	14.527	-6.733	41.081	1.00 39.50
ATOM	2338	OH2	WAT	658	12.344	-8.188	-4.840	1.00 31.36
ATOM	2339	OH2	WAT	659	2.335	0.119	-12.679	1.00 46.96
ATOM	2340	OH2	WAT	660	-4.072	8.903	35.840	1.00 33.73
ATOM	2341	OH2	WAT	661	11.199	-3.361	13.690	1.00 30.89
ATOM	2342	OH2	WAT	662	33.630	13.397	20.072	1.00 32.18
ATOM	2343	OH2	WAT	663	-8.225	5.595	20.237	1.00 42.51
ATOM	2344	OH2	WAT	664	4.851	8.191	41.111	1.00 38.06
ATOM	2345	OH2	WAT	665	9.375	6.937	-3.912	1.00 45.24
ATOM	2346	OH2	WAT	666	16.913	-0.045	-10.717	1.00 42.04
ATOM	2347	OH2	WAT	667	29.488	-4.757	36.815	1.00 47.43
ATOM	2348	OH2	WAT	668	23.202	16.279	14.705	1.00 36.53
ATOM	2349	OH2	WAT	669	1.557	-10.157	34.020	1.00 34.64
ATOM	2350	OH2	WAT	670	30.193	6.969	18.404	1.00 43.94
ATOM	2351	OH2	WAT	671	9.581	18.649	26.362	1.00 38.51
ATOM	2352	OH2	WAT	672	3.957	11.310	37.024	1.00 42.49

FIG.11A-56

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ATOM   2353  OH2 WAT   673      23.314 -12.393  29.627  1.00 44.03
ATOM   2354  OH2 WAT   674      29.567  -4.326  22.984  1.00 38.54
ATOM   2355  OH2 WAT   675      20.341 -13.530  33.695  1.00 35.66
ATOM   2356  OH2 WAT   676      24.115  -2.262  12.332  1.00 24.55
ATOM   2357  OH2 WAT   677      21.496  16.243  18.532  1.00 38.18
ATOM   2358  OH2 WAT   678       1.474  14.677  18.946  1.00 34.15
ATOM   2359  OH2 WAT   679      22.623  10.998  43.542  1.00 34.98
ATOM   2360  OH2 WAT   680      22.204   4.868  42.384  1.00 35.66
ATOM   2361  OH2 WAT   681       4.974  18.238  22.943  1.00 43.25
ATOM   2362  OH2 WAT   682       7.600  17.266  28.095  1.00 47.36
ATOM   2363  OH2 WAT   683       9.887  -4.665  20.529  1.00 55.08
ATOM   2364  OH2 WAT   684      34.174  16.468  30.910  1.00 59.36
ATOM   2365  OH2 WAT   685      14.332  -9.413  41.717  1.00 44.97
ATOM   2366  OH2 WAT   686      -6.650  -2.511  31.135  1.00 56.20
ATOM   2367  OH2 WAT   687       3.069  14.962  28.974  1.00 53.45
ATOM   2368  S   SO4   901      -0.036  -4.899  27.988  1.00 27.31
ATOM   2369  O1  SO4   901       0.702  -5.486  26.855  1.00 27.32
ATOM   2370  O2  SO4   901       0.883  -4.694  29.123  1.00 30.06
ATOM   2371  O3  SO4   901      -1.115  -5.818  28.406  1.00 25.85
ATOM   2372  O4  SO4   901      -0.628  -3.611  27.579  1.00 30.90
END
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FIG.11A-57

ATOM	1	CB	ALA	2	-1.758	8.559	-13.637	1.00	37.12
ATOM	2	C	ALA	2	0.707	8.098	-13.520	1.00	36.78
ATOM	3	O	ALA	2	0.588	7.652	-14.662	1.00	37.76
ATOM	4	N	ALA	2	-0.253	10.204	-12.575	1.00	37.69
ATOM	5	CA	ALA	2	-0.489	8.748	-12.807	1.00	37.30
ATOM	6	N	VAL	3	1.848	8.047	-12.838	1.00	35.55
ATOM	7	CA	VAL	3	3.063	7.454	-13.398	1.00	34.24
ATOM	8	CB	VAL	3	4.313	7.955	-12.643	1.00	34.18
ATOM	9	CG1	VAL	3	5.571	7.440	-13.323	1.00	34.29
ATOM	10	CG2	VAL	3	4.317	9.475	-12.588	1.00	34.68
ATOM	11	C	VAL	3	2.978	5.903	-13.310	1.00	33.32
ATOM	12	O	VAL	3	2.931	5.330	-12.229	1.00	32.18
ATOM	13	N	PRO	4	2.991	5.224	-14.464	1.00	31.94
ATOM	14	CD	PRO	4	3.225	5.848	-15.781	1.00	31.07
ATOM	15	CA	PRO	4	2.907	3.767	-14.603	1.00	32.30
ATOM	16	CB	PRO	4	3.523	3.536	-15.977	1.00	31.18
ATOM	17	CG	PRO	4	2.992	4.691	-16.737	1.00	30.95
ATOM	18	C	PRO	4	3.439	2.787	-13.560	1.00	32.70
ATOM	19	O	PRO	4	2.692	1.913	-13.099	1.00	34.83
ATOM	20	N	PHE	5	4.703	2.917	-13.182	1.00	31.29
ATOM	21	CA	PHE	5	5.317	1.949	-12.268	1.00	29.35
ATOM	22	CB	PHE	5	6.565	1.362	-12.934	1.00	27.15
ATOM	23	CG	PHE	5	6.385	1.053	-14.399	1.00	22.94
ATOM	24	CD1	PHE	5	7.159	1.694	-15.365	1.00	22.19
ATOM	25	CD2	PHE	5	5.455	0.112	-14.812	1.00	21.56
ATOM	26	CE1	PHE	5	7.001	1.390	-16.724	1.00	20.64
ATOM	27	CE2	PHE	5	5.289	-0.198	-16.162	1.00	20.80
ATOM	28	CZ	PHE	5	6.067	0.444	-17.119	1.00	20.05
ATOM	29	C	PHE	5	5.770	2.421	-10.879	1.00	29.91
ATOM	30	O	PHE	5	6.569	1.742	-10.226	1.00	29.38
ATOM	31	N	VAL	6	5.261	3.559	-10.428	1.00	30.15
ATOM	32	CA	VAL	6	5.665	4.110	-9.137	1.00	30.31
ATOM	33	CB	VAL	6	5.120	5.548	-8.959	1.00	30.49
ATOM	34	CG1	VAL	6	5.730	6.201	-7.727	1.00	30.84
ATOM	35	CG2	VAL	6	5.439	6.368	-10.181	1.00	30.64
ATOM	36	C	VAL	6	5.270	3.291	-7.898	1.00	30.97
ATOM	37	O	VAL	6	5.731	3.579	-6.792	1.00	30.99
ATOM	38	N	GLU	7	4.441	2.268	-8.074	1.00	30.81
ATOM	39	CA	GLU	7	4.023	1.465	-6.929	1.00	30.96
ATOM	40	CB	GLU	7	2.536	1.131	-7.032	1.00	33.16
ATOM	41	CG	GLU	7	1.797	2.481	-6.822	1.00	35.64

FIG.11B-1

ATOM	42	CD	GLU	7	2.340	3.275	-5.622	1.00	37.65
ATOM	43	OE1	GLU	7	3.400	3.921	-5.755	1.00	38.88
ATOM	44	OE2	GLU	7	1.728	3.259	-4.532	1.00	37.93
ATOM	45	C	GLU	7	4.819	0.213	-6.723	1.00	29.89
ATOM	46	O	GLU	7	4.546	-0.563	-5.806	1.00	28.91
ATOM	47	N	ASP	8	5.827	0.010	-7.566	1.00	27.92
ATOM	48	CA	ASP	8	6.671	-1.163	-7.451	1.00	26.87
ATOM	49	CB	ASP	8	7.122	-1.675	-8.820	1.00	27.02
ATOM	50	CG	ASP	8	5.988	-2.243	-9.636	1.00	28.55
ATOM	51	OD1	ASP	8	5.115	-2.957	-9.092	1.00	28.96
ATOM	52	OD2	ASP	8	5.984	-1.978	-10.856	1.00	29.04
ATOM	53	C	ASP	8	7.902	-0.881	-6.651	1.00	26.17
ATOM	54	O	ASP	8	8.599	0.112	-6.880	1.00	25.38
ATOM	55	N	TRP	9	8.165	-1.767	-5.698	1.00	25.50
ATOM	56	CA	TRP	9	9.316	-1.674	-4.814	1.00	25.48
ATOM	57	CB	TRP	9	8.856	-1.476	-3.360	1.00	26.35
ATOM	58	CG	TRP	9	8.975	-0.060	-2.872	1.00	27.81
ATOM	59	CD2	TRP	9	7.939	0.920	-2.829	1.00	27.99
ATOM	60	CE2	TRP	9	8.511	2.110	-2.324	1.00	28.08
ATOM	61	CE3	TRP	9	6.580	0.910	-3.169	1.00	27.50
ATOM	62	CD1	TRP	9	10.108	0.557	-2.404	1.00	28.28
ATOM	63	NE1	TRP	9	9.837	1.860	-2.074	1.00	27.98
ATOM	64	CZ2	TRP	9	7.775	3.279	-2.150	1.00	27.32
ATOM	65	CZ3	TRP	9	5.848	2.070	-2.996	1.00	29.26
ATOM	66	CH2	TRP	9	6.447	3.243	-2.488	1.00	29.79
ATOM	67	C	TRP	9	10.129	-2.960	-4.877	1.00	25.40
ATOM	68	O	TRP	9	9.634	-4.028	-4.523	1.00	25.51
ATOM	69	N	ASP	10	11.374	-2.857	-5.328	1.00	24.86
ATOM	70	CA	ASP	10	12.260	-4.015	-5.414	1.00	25.35
ATOM	71	CB	ASP	10	13.412	-3.734	-6.381	1.00	25.70
ATOM	72	CG	ASP	10	12.908	-3.616	-7.816	1.00	26.56
ATOM	73	OD1	ASP	10	13.473	-2.799	-8.588	1.00	27.18
ATOM	74	OD2	ASP	10	11.959	-4.361	-8.157	1.00	26.29
ATOM	75	C	ASP	10	12.875	-4.328	-4.035	1.00	26.53
ATOM	76	O	ASP	10	13.358	-3.426	-3.342	1.00	25.47
ATOM	77	N	LEU	11	12.836	-5.602	-3.645	1.00	27.39
ATOM	78	CA	LEU	11	13.415	-6.041	-2.373	1.00	29.13
ATOM	79	CB	LEU	11	12.585	-7.191	-1.780	1.00	29.22
ATOM	80	CG	LEU	11	11.165	-6.817	-1.329	1.00	29.89
ATOM	81	CD1	LEU	11	10.370	-6.260	-2.494	1.00	31.00
ATOM	82	CD2	LEU	11	10.463	-8.052	-0.768	1.00	29.99
ATOM	83	C	LEU	11	14.828	-6.461	-2.720	1.00	30.25

FIG.11B-2

ATOM	84	O	LEU	11	15.058	-7.557	-3.235	1.00	30.42
ATOM	85	N	VAL	12	15.783	-5.581	-2.436	1.00	31.49
ATOM	86	CA	VAL	12	17.176	-5.813	-2.797	1.00	32.51
ATOM	87	CB	VAL	12	17.798	-4.495	-3.312	1.00	33.09
ATOM	88	CG1	VAL	12	19.207	-4.740	-3.855	1.00	34.30
ATOM	89	CG2	VAL	12	16.907	-3.905	-4.400	1.00	33.06
ATOM	90	C	VAL	12	18.130	-6.437	-1.774	1.00	33.49
ATOM	91	O	VAL	12	19.202	-6.906	-2.151	1.00	33.55
ATOM	92	N	GLN	13	17.767	-6.444	-0.495	1.00	34.17
ATOM	93	CA	GLN	13	18.646	-7.043	0.511	1.00	35.23
ATOM	94	CB	GLN	13	19.962	-6.269	0.625	1.00	36.13
ATOM	95	CG	GLN	13	19.957	-4.746	0.685	1.00	37.34
ATOM	96	CD	GLN	13	21.380	-4.268	0.950	1.00	38.25
ATOM	97	OE1	GLN	13	21.930	-4.495	2.029	1.00	38.73
ATOM	98	NE2	GLN	13	21.981	-3.608	-0.039	1.00	39.12
ATOM	99	C	GLN	13	18.064	-7.158	1.892	1.00	35.56
ATOM	100	O	GLN	13	17.359	-6.266	2.362	1.00	35.04
ATOM	101	N	THR	14	18.359	-8.275	2.549	1.00	36.12
ATOM	102	CA	THR	14	17.871	-8.516	3.901	1.00	37.26
ATOM	103	CB	THR	14	18.035	-9.992	4.309	1.00	37.85
ATOM	104	OG1	THR	14	17.689	-10.148	5.691	1.00	39.17
ATOM	105	CG2	THR	14	19.471	-10.442	4.102	1.00	38.49
ATOM	106	C	THR	14	18.653	-7.673	4.879	1.00	37.46
ATOM	107	O	THR	14	19.864	-7.503	4.737	1.00	37.37
ATOM	108	N	LEU	15	17.961	-7.130	5.872	1.00	37.76
ATOM	109	CA	LEU	15	18.604	-6.302	6.884	1.00	38.54
ATOM	110	CB	LEU	15	17.827	-5.003	7.100	1.00	38.69
ATOM	111	CG	LEU	15	17.768	-4.000	5.946	1.00	38.81
ATOM	112	CD1	LEU	15	19.162	-3.533	5.539	1.00	38.58
ATOM	113	CD2	LEU	15	17.075	-4.674	4.787	1.00	39.25
ATOM	114	C	LEU	15	18.662	-7.039	8.201	1.00	39.26
ATOM	115	O	LEU	15	19.189	-6.528	9.190	1.00	39.06
ATOM	116	N	GLY	16	18.112	-8.248	8.210	1.00	40.02
ATOM	117	CA	GLY	16	18.101	-9.054	9.416	1.00	41.67
ATOM	118	C	GLY	16	16.767	-9.752	9.569	1.00	42.84
ATOM	119	O	GLY	16	15.726	-9.165	9.280	1.00	43.09
ATOM	120	N	GLU	17	16.791	-11.003	10.024	1.00	43.99
ATOM	121	CA	GLU	17	15.564	-11.775	10.203	1.00	44.96
ATOM	122	CB	GLU	17	15.744	-13.210	9.707	1.00	45.76
ATOM	123	CG	GLU	17	16.145	-13.419	8.237	1.00	46.77
ATOM	124	CD	GLU	17	16.308	-14.915	8.042	1.00	47.36
ATOM	125	OE1	GLU	17	17.089	-15.524	8.805	1.00	47.74

FIG.11B-3

ATOM	126	OE2	GLU	17	15.667	-15.486	7.134	1.00	48.12
ATOM	127	C	GLU	17	15.131	-11.854	11.664	1.00	45.33
ATOM	128	O	GLU	17	15.952	-11.725	12.576	1.00	45.16
ATOM	129	N	GLY	18	13.835	-12.066	11.872	1.00	45.83
ATOM	130	CA	GLY	18	13.296	-12.170	13.216	1.00	46.41
ATOM	131	C	GLY	18	12.627	-13.515	13.409	1.00	46.60
ATOM	132	O	GLY	18	12.340	-14.212	12.437	1.00	46.89
ATOM	133	N	ALA	19	12.376	-13.880	14.663	1.00	46.88
ATOM	134	CA	ALA	19	11.745	-15.155	14.977	1.00	46.85
ATOM	135	CB	ALA	19	11.695	-15.350	16.492	1.00	46.77
ATOM	136	C	ALA	19	10.342	-15.268	14.390	1.00	46.78
ATOM	137	O	ALA	19	9.701	-16.310	14.505	1.00	47.08
ATOM	138	N	TYR	20	9.867	-14.196	13.763	1.00	46.62
ATOM	139	CA	TYR	20	8.533	-14.187	13.165	1.00	46.18
ATOM	140	CB	TYR	20	7.504	-13.682	14.185	1.00	46.74
ATOM	141	CG	TYR	20	8.056	-12.671	15.169	1.00	47.27
ATOM	142	CD1	TYR	20	8.661	-11.493	14.728	1.00	47.21
ATOM	143	CE1	TYR	20	9.195	-10.576	15.629	1.00	47.56
ATOM	144	CD2	TYR	20	7.994	-12.904	16.544	1.00	47.53
ATOM	145	CE2	TYR	20	8.524	-11.993	17.454	1.00	47.75
ATOM	146	CZ	TYR	20	9.125	-10.833	16.990	1.00	47.80
ATOM	147	OH	TYR	20	9.673	-9.940	17.884	1.00	48.14
ATOM	148	C	TYR	20	8.449	-13.336	11.886	1.00	45.48
ATOM	149	O	TYR	20	7.509	-12.557	11.708	1.00	45.95
ATOM	150	N	GLY	21	9.432	-13.496	11.004	1.00	44.27
ATOM	151	CA	GLY	21	9.441	-12.742	9.761	1.00	42.92
ATOM	152	C	GLY	21	10.817	-12.250	9.349	1.00	41.50
ATOM	153	O	GLY	21	11.833	-12.774	9.800	1.00	41.92
ATOM	154	N	GLU	22	10.850	-11.236	8.489	1.00	40.28
ATOM	155	CA	GLU	22	12.111	-10.671	8.012	1.00	38.41
ATOM	156	CB	GLU	22	12.571	-11.389	6.736	1.00	39.39
ATOM	157	CG	GLU	22	11.451	-11.244	5.667	1.00	40.60
ATOM	158	CD	GLU	22	11.755	-11.845	4.292	1.00	41.48
ATOM	159	OE1	GLU	22	10.825	-11.842	3.459	1.00	42.22
ATOM	160	OE2	GLU	22	12.882	-12.309	4.019	1.00	42.38
ATOM	161	C	GLU	22	11.967	-9.174	7.684	1.00	36.25
ATOM	162	O	GLU	22	10.858	-8.655	7.577	1.00	36.15
ATOM	163	N	VAL	23	13.098	-8.497	7.537	1.00	34.42
ATOM	164	CA	VAL	23	13.116	-7.077	7.198	1.00	32.22
ATOM	165	CB	VAL	23	13.731	-6.227	8.338	1.00	32.25
ATOM	166	CG1	VAL	23	13.708	-4.749	7.965	1.00	30.96
ATOM	167	CG2	VAL	23	12.958	-6.456	9.622	1.00	31.12

FIG.11B-4

ATOM	168	C	VAL	23	13.967	-6.926	5.945	1.00	31.31
ATOM	169	O	VAL	23	15.121	-7.343	5.915	1.00	30.82
ATOM	170	N	GLN	24	13.389	-6.335	4.909	1.00	30.37
ATOM	171	CA	GLN	24	14.093	-6.148	3.647	1.00	29.94
ATOM	172	CB	GLN	24	13.339	-6.832	2.504	1.00	31.05
ATOM	173	CG	GLN	24	13.176	-8.363	2.473	1.00	33.39
ATOM	174	CD	GLN	24	14.549	-8.990	2.258	1.00	34.46
ATOM	175	OE1	GLN	24	15.284	-8.607	1.342	1.00	35.21
ATOM	176	NE2	GLN	24	14.896	-9.958	3.101	1.00	35.38
ATOM	177	C	GLN	24	14.224	-4.699	3.268	1.00	28.82
ATOM	178	O	GLN	24	13.376	-3.878	3.612	1.00	28.38
ATOM	179	N	LEU	25	15.301	-4.374	2.559	1.00	27.94
ATOM	180	CA	LEU	25	15.515	-3.015	2.086	1.00	27.18
ATOM	181	CB	LEU	25	17.008	-2.729	1.878	1.00	28.17
ATOM	182	CG	LEU	25	17.457	-1.432	1.183	1.00	29.19
ATOM	183	CD1	LEU	25	17.192	-1.511	-0.302	1.00	31.15
ATOM	184	CD2	LEU	25	16.728	-0.244	1.790	1.00	29.21
ATOM	185	C	LEU	25	14.808	-2.978	0.765	1.00	26.32
ATOM	186	O	LEU	25	15.078	-3.808	-0.103	1.00	26.83
ATOM	187	N	ALA	26	13.886	-2.037	0.608	1.00	25.18
ATOM	188	CA	ALA	26	13.134	-1.921	-0.635	1.00	23.91
ATOM	189	CB	ALA	26	11.638	-1.992	-0.351	1.00	24.21
ATOM	190	C	ALA	26	13.464	-0.641	-1.335	1.00	23.39
ATOM	191	O	ALA	26	13.543	0.414	-0.713	1.00	23.17
ATOM	192	N	VAL	27	13.646	-0.719	-2.648	1.00	22.24
ATOM	193	CA	VAL	27	13.979	0.460	-3.433	1.00	21.16
ATOM	194	CB	VAL	27	15.397	0.311	-4.031	1.00	21.43
ATOM	195	CG1	VAL	27	15.735	1.514	-4.896	1.00	21.22
ATOM	196	CG2	VAL	27	16.422	0.177	-2.900	1.00	20.94
ATOM	197	C	VAL	27	12.926	0.626	-4.503	1.00	20.42
ATOM	198	O	VAL	27	12.603	-0.320	-5.223	1.00	20.31
ATOM	199	N	ASN	28	12.381	1.831	-4.606	1.00	19.21
ATOM	200	CA	ASN	28	11.331	2.108	-5.575	1.00	18.90
ATOM	201	CB	ASN	28	10.775	3.511	-5.343	1.00	19.28
ATOM	202	CG	ASN	28	9.535	3.680	-6.151	1.00	19.66
ATOM	203	OD1	ASN	28	9.584	4.128	-7.294	1.00	18.90
ATOM	204	ND2	ASN	28	8.394	3.313	-5.574	1.00	20.03
ATOM	205	C	ASN	28	11.834	1.962	-6.985	1.00	18.62
ATOM	206	O	ASN	28	12.893	2.482	-7.343	1.00	19.04
ATOM	207	N	ARG	29	11.062	1.253	-7.797	1.00	17.64
ATOM	208	CA	ARG	29	11.440	1.009	-9.185	1.00	17.42
ATOM	209	CB	ARG	29	10.344	0.191	-9.860	1.00	17.14

FIG. 11B-5

ATOM	210	CG	ARG	29	10.521	0.026	-11.359	1.00	16.26
ATOM	211	CD	ARG	29	9.318	-0.788	-11.804	1.00	15.93
ATOM	212	NE	ARG	29	9.278	-0.897	-13.267	1.00	14.41
ATOM	213	CZ	ARG	29	8.410	-1.645	-13.940	1.00	16.02
ATOM	214	NH1	ARG	29	7.484	-2.359	-13.289	1.00	17.06
ATOM	215	NH2	ARG	29	8.481	-1.699	-15.267	1.00	15.37
ATOM	216	C	ARG	29	11.684	2.279	-9.978	1.00	18.14
ATOM	217	O	ARG	29	12.641	2.364	-10.759	1.00	18.01
ATOM	218	N	VAL	30	10.821	3.266	-9.769	1.00	18.31
ATOM	219	CA	VAL	30	10.901	4.540	-10.477	1.00	18.70
ATOM	220	CB	VAL	30	9.492	5.153	-10.639	1.00	18.65
ATOM	221	CG1	VAL	30	9.587	6.584	-11.138	1.00	18.77
ATOM	222	CG2	VAL	30	8.653	4.297	-11.581	1.00	17.98
ATOM	223	C	VAL	30	11.797	5.605	-9.819	1.00	18.99
ATOM	224	O	VAL	30	12.723	6.110	-10.444	1.00	19.65
ATOM	225	N	THR	31	11.527	5.930	-8.555	1.00	19.32
ATOM	226	CA	THR	31	12.277	6.980	-7.868	1.00	20.78
ATOM	227	CB	THR	31	11.406	7.701	-6.820	1.00	21.46
ATOM	228	OG1	THR	31	11.118	6.801	-5.742	1.00	21.87
ATOM	229	CG2	THR	31	10.110	8.198	-7.448	1.00	21.89
ATOM	230	C	THR	31	13.559	6.616	-7.144	1.00	20.65
ATOM	231	O	THR	31	14.339	7.507	-6.784	1.00	20.94
ATOM	232	N	GLU	32	13.767	5.319	-6.934	1.00	21.15
ATOM	233	CA	GLU	32	14.927	4.772	-6.238	1.00	21.92
ATOM	234	CB	GLU	32	16.239	5.257	-6.861	1.00	23.54
ATOM	235	CG	GLU	32	16.258	4.557	-8.256	1.00	25.53
ATOM	236	CD	GLU	32	17.606	4.686	-8.924	1.00	27.14
ATOM	237	OE1	GLU	32	18.624	4.258	-8.330	1.00	29.51
ATOM	238	OE2	GLU	32	17.636	5.212	-10.049	1.00	26.82
ATOM	239	C	GLU	32	14.912	5.113	-4.755	1.00	22.53
ATOM	240	O	GLU	32	15.918	4.948	-4.067	1.00	21.93
ATOM	241	N	GLU	33	13.770	5.584	-4.271	1.00	23.56
ATOM	242	CA	GLU	33	13.632	5.907	-2.851	1.00	25.27
ATOM	243	CB	GLU	33	12.281	6.581	-2.581	1.00	27.64
ATOM	244	CG	GLU	33	11.945	6.632	-1.055	1.00	30.98
ATOM	245	CD	GLU	33	10.594	7.270	-0.711	1.00	32.85
ATOM	246	OE1	GLU	33	9.689	7.294	-1.571	1.00	34.30
ATOM	247	OE2	GLU	33	10.425	7.742	0.437	1.00	35.48
ATOM	248	C	GLU	33	13.727	4.575	-2.097	1.00	24.84
ATOM	249	O	GLU	33	13.229	3.546	-2.575	1.00	23.78
ATOM	250	N	ALA	34	14.373	4.595	-0.931	1.00	24.67
ATOM	251	CA	ALA	34	14.537	3.388	-0.132	1.00	25.43

FIG.11B-6

ATOM	252	CB	ALA	34	16.006	3.207	0.244	1.00	25.80
ATOM	253	C	ALA	34	13.694	3.404	1.125	1.00	25.49
ATOM	254	O	ALA	34	13.559	4.435	1.785	1.00	25.71
ATOM	255	N	VAL	35	13.117	2.254	1.449	1.00	25.20
ATOM	256	CA	VAL	35	12.324	2.110	2.666	1.00	25.48
ATOM	257	CB	VAL	35	10.799	2.237	2.414	1.00	25.90
ATOM	258	CG1	VAL	35	10.461	3.621	1.870	1.00	25.96
ATOM	259	CG2	VAL	35	10.339	1.150	1.467	1.00	27.05
ATOM	260	C	VAL	35	12.585	0.738	3.180	1.00	25.10
ATOM	261	O	VAL	35	13.041	-0.129	2.433	1.00	25.54
ATOM	262	N	ALA	36	12.324	0.521	4.465	1.00	24.18
ATOM	263	CA	ALA	36	12.503	-0.793	5.058	1.00	23.82
ATOM	264	CB	ALA	36	13.081	-0.671	6.479	1.00	23.63
ATOM	265	C	ALA	36	11.143	-1.443	5.099	1.00	24.17
ATOM	266	O	ALA	36	10.147	-0.807	5.451	1.00	23.23
ATOM	267	N	VAL	37	11.087	-2.714	4.719	1.00	24.59
ATOM	268	CA	VAL	37	9.832	-3.439	4.718	1.00	25.64
ATOM	269	CB	VAL	37	9.506	-4.006	3.316	1.00	25.94
ATOM	270	CG1	VAL	37	8.174	-4.755	3.356	1.00	25.77
ATOM	271	CG2	VAL	37	9.453	-2.870	2.311	1.00	26.82
ATOM	272	C	VAL	37	9.915	-4.556	5.683	1.00	26.26
ATOM	273	O	VAL	37	10.724	-5.462	5.532	1.00	25.86
ATOM	274	N	LYS	38	9.091	-4.489	6.716	1.00	27.45
ATOM	275	CA	LYS	38	9.066	-5.534	7.725	1.00	29.32
ATOM	276	CB	LYS	38	8.729	-4.923	9.091	1.00	29.33
ATOM	277	CG	LYS	38	8.764	-5.913	10.243	1.00	30.35
ATOM	278	CD	LYS	38	8.546	-5.119	11.550	1.00	30.39
ATOM	279	CE	LYS	38	8.715	-5.997	12.796	1.00	30.62
ATOM	280	NZ	LYS	38	8.705	-5.183	14.038	1.00	29.08
ATOM	281	C	LYS	38	8.007	-6.537	7.295	1.00	30.44
ATOM	282	O	LYS	38	6.824	-6.212	7.247	1.00	30.48
ATOM	283	N	ILE	39	8.443	-7.748	6.964	1.00	32.39
ATOM	284	CA	ILE	39	7.539	-8.805	6.528	1.00	34.05
ATOM	285	CB	ILE	39	8.130	-9.560	5.322	1.00	34.69
ATOM	286	CG2	ILE	39	7.073	-10.462	4.702	1.00	34.87
ATOM	287	CG1	ILE	39	8.603	-8.553	4.271	1.00	34.64
ATOM	288	CD1	ILE	39	9.193	-9.188	3.005	1.00	35.49
ATOM	289	C	ILE	39	7.295	-9.775	7.672	1.00	35.39
ATOM	290	O	ILE	39	8.238	-10.291	8.273	1.00	35.78
ATOM	291	N	VAL	40	6.025	-10.018	7.977	1.00	36.68
ATOM	292	CA	VAL	40	5.672	-10.919	9.069	1.00	38.18
ATOM	293	CB	VAL	40	5.304	-10.116	10.337	1.00	38.57

FIG.11B-7

ATOM	294	CG1	VAL	40	6.530	-9.382	10.863	1.00	38.14
ATOM	295	CG2	VAL	40	4.204	-9.118	10.019	1.00	38.65
ATOM	296	C	VAL	40	4.514	-11.850	8.710	1.00	39.27
ATOM	297	O	VAL	40	3.393	-11.401	8.470	1.00	39.49
ATOM	298	N	ASP	41	4.794	-13.150	8.678	1.00	40.75
ATOM	299	CA	ASP	41	3.772	-14.145	8.355	1.00	42.21
ATOM	300	CB	ASP	41	4.412	-15.507	8.078	1.00	42.73
ATOM	301	CG	ASP	41	3.334	-16.461	7.562	1.00	43.32
ATOM	302	OD1	ASP	41	2.325	-16.676	8.268	1.00	44.00
ATOM	303	OD2	ASP	41	3.499	-16.997	6.445	1.00	43.83
ATOM	304	C	ASP	41	2.790	-14.290	9.515	1.00	42.79
ATOM	305	O	ASP	41	3.155	-14.759	10.596	1.00	43.26
ATOM	306	N	MET	42	1.542	-13.895	9.278	1.00	43.17
ATOM	307	CA	MET	42	0.495	-13.954	10.295	1.00	43.48
ATOM	308	CB	MET	42	-0.859	-13.567	9.690	1.00	44.53
ATOM	309	CG	MET	42	-0.894	-12.152	9.054	1.00	45.50
ATOM	310	SD	MET	42	-2.480	-11.758	8.271	1.00	47.53
ATOM	311	CE	MET	42	-3.298	-10.869	9.602	1.00	45.69
ATOM	312	C	MET	42	0.324	-15.322	10.981	1.00	43.53
ATOM	313	O	MET	42	-0.488	-15.458	11.898	1.00	43.38
ATOM	314	N	ALA	43	1.087	-16.320	10.543	1.00	43.07
ATOM	315	CA	ALA	43	0.991	-17.656	11.125	1.00	43.42
ATOM	316	CB	ALA	43	-0.040	-18.484	10.359	1.00	43.10
ATOM	317	C	ALA	43	2.327	-18.378	11.137	1.00	43.21
ATOM	318	O	ALA	43	2.386	-19.594	10.955	1.00	43.78
ATOM	319	N	ALA	44	3.403	-17.633	11.357	1.00	42.71
ATOM	320	CA	ALA	44	4.733	-18.227	11.388	1.00	42.36
ATOM	321	CB	ALA	44	5.750	-17.260	10.792	1.00	41.81
ATOM	322	C	ALA	44	5.117	-18.581	12.817	1.00	42.44
ATOM	323	O	ALA	44	6.254	-18.285	13.244	1.00	42.57
ATOM	324	OT	ALA	44	4.263	-19.178	13.504	1.00	42.66
ATOM	325	CB	CYS	48	0.655	-13.396	16.575	1.00	44.68
ATOM	326	SG	CYS	48	-0.887	-13.047	17.451	1.00	46.03
ATOM	327	C	CYS	48	-0.464	-12.204	14.719	1.00	43.08
ATOM	328	O	CYS	48	0.015	-11.080	14.888	1.00	42.59
ATOM	329	N	CYS	48	1.582	-13.589	14.278	1.00	42.75
ATOM	330	CA	CYS	48	0.332	-13.460	15.083	1.00	43.49
ATOM	331	N	PRO	49	-1.700	-12.387	14.224	1.00	42.07
ATOM	332	CD	PRO	49	-2.344	-13.692	13.989	1.00	42.03
ATOM	333	CA	PRO	49	-2.591	-11.294	13.824	1.00	42.17
ATOM	334	CB	PRO	49	-3.891	-12.028	13.488	1.00	42.12
ATOM	335	CG	PRO	49	-3.406	-13.342	12.979	1.00	41.95

FIG.11B-8

ATOM	336	C	PRO	49	-2.745	-10.224	14.887	1.00	41.81
ATOM	337	O	PRO	49	-2.664	-9.031	14.592	1.00	42.45
ATOM	338	N	GLU	50	-2.969	-10.652	16.126	1.00	41.02
ATOM	339	CA	GLU	50	-3.156	-9.729	17.246	1.00	39.67
ATOM	340	CB	GLU	50	-3.526	-10.488	18.522	1.00	40.23
ATOM	341	CG	GLU	50	-3.682	-9.495	19.715	1.00	40.60
ATOM	342	CD	GLU	50	-3.534	-10.215	21.053	1.00	41.12
ATOM	343	OE1	GLU	50	-2.452	-10.793	21.314	1.00	42.36
ATOM	344	OE2	GLU	50	-4.504	-10.196	21.839	1.00	42.30
ATOM	345	C	GLU	50	-1.926	-8.886	17.586	1.00	38.68
ATOM	346	O	GLU	50	-2.025	-7.666	17.747	1.00	38.74
ATOM	347	N	ALA	51	-0.775	-9.542	17.714	1.00	37.63
ATOM	348	CA	ALA	51	0.468	-8.856	18.055	1.00	36.16
ATOM	349	CB	ALA	51	1.591	-9.872	18.236	1.00	36.72
ATOM	350	C	ALA	51	0.863	-7.832	17.010	1.00	35.47
ATOM	351	O	ALA	51	1.150	-6.675	17.330	1.00	34.50
ATOM	352	N	ILE	52	0.885	-8.260	15.754	1.00	34.45
ATOM	353	CA	ILE	52	1.248	-7.370	14.664	1.00	33.77
ATOM	354	CB	ILE	52	1.420	-8.194	13.354	1.00	34.35
ATOM	355	CG2	ILE	52	0.066	-8.432	12.708	1.00	34.21
ATOM	356	CG1	ILE	52	2.451	-7.522	12.440	1.00	34.69
ATOM	357	CD1	ILE	52	2.122	-6.082	12.050	1.00	35.78
ATOM	358	C	ILE	52	0.158	-6.248	14.543	1.00	33.00
ATOM	359	O	ILE	52	0.462	-5.095	14.214	1.00	32.57
ATOM	360	N	LYS	53	-1.092	-6.600	14.826	1.00	32.29
ATOM	361	CA	LYS	53	-2.177	-5.627	14.744	1.00	31.31
ATOM	362	CB	LYS	53	-3.520	-6.275	15.097	1.00	32.79
ATOM	363	CG	LYS	53	-4.591	-5.745	14.135	1.00	35.30
ATOM	364	CD	LYS	53	-4.333	-6.330	12.710	1.00	36.83
ATOM	365	CE	LYS	53	-5.147	-5.687	11.568	1.00	37.66
ATOM	366	NZ	LYS	53	-4.748	-4.262	11.361	1.00	39.01
ATOM	367	C	LYS	53	-1.922	-4.469	15.733	1.00	29.81
ATOM	368	O	LYS	53	-2.123	-3.297	15.410	1.00	29.51
ATOM	369	N	LYS	54	-1.471	-4.810	16.933	1.00	28.14
ATOM	370	CA	LYS	54	-1.202	-3.801	17.942	1.00	26.62
ATOM	371	CB	LYS	54	-0.984	-4.475	19.292	1.00	26.85
ATOM	372	CG	LYS	54	-0.815	-3.468	20.426	1.00	26.40
ATOM	373	CD	LYS	54	-0.807	-4.242	21.744	1.00	27.28
ATOM	374	CE	LYS	54	-0.732	-3.338	22.970	1.00	27.15
ATOM	375	NZ	LYS	54	-0.636	-4.143	24.224	1.00	27.93
ATOM	376	C	LYS	54	0.008	-2.953	17.542	1.00	25.67
ATOM	377	O	LYS	54	0.027	-1.738	17.751	1.00	25.37

FIG.11B-9

ATOM	378	N	GLU	55	1.010	-3.599	16.950	1.00	24.57
ATOM	379	CA	GLU	55	2.210	-2.892	16.517	1.00	22.90
ATOM	380	CB	GLU	55	3.246	-3.892	15.987	1.00	22.70
ATOM	381	CG	GLU	55	4.551	-3.198	15.516	1.00	22.01
ATOM	382	CD	GLU	55	5.645	-4.208	15.112	1.00	22.15
ATOM	383	OE1	GLU	55	5.523	-5.412	15.423	1.00	23.29
ATOM	384	OE2	GLU	55	6.643	-3.798	14.487	1.00	22.01
ATOM	385	C	GLU	55	1.842	-1.857	15.436	1.00	22.77
ATOM	386	O	GLU	55	2.387	-0.756	15.399	1.00	21.95
ATOM	387	N	ILE	56	0.898	-2.215	14.570	1.00	22.54
ATOM	388	CA	ILE	56	0.467	-1.320	13.507	1.00	22.45
ATOM	389	CB	ILE	56	-0.378	-2.105	12.475	1.00	23.28
ATOM	390	CG2	ILE	56	-0.995	-1.170	11.459	1.00	23.81
ATOM	391	CG1	ILE	56	0.516	-3.127	11.778	1.00	22.95
ATOM	392	CD1	ILE	56	-0.237	-4.041	10.775	1.00	23.35
ATOM	393	C	ILE	56	-0.299	-0.174	14.087	1.00	22.53
ATOM	394	O	ILE	56	-0.092	0.979	13.712	1.00	22.30
ATOM	395	N	CYS	57	-1.179	-0.493	15.030	1.00	22.44
ATOM	396	CA	CYS	57	-2.008	0.497	15.709	1.00	23.00
ATOM	397	CB	CYS	57	-2.832	-0.188	16.804	1.00	23.58
ATOM	398	SG	CYS	57	-3.925	0.986	17.618	1.00	26.04
ATOM	399	C	CYS	57	-1.157	1.603	16.347	1.00	22.83
ATOM	400	O	CYS	57	-1.441	2.795	16.203	1.00	23.71
ATOM	401	N	ILE	58	-0.115	1.187	17.055	1.00	21.58
ATOM	402	CA	ILE	58	0.757	2.129	17.725	1.00	20.88
ATOM	403	CB	ILE	58	1.594	1.391	18.786	1.00	21.07
ATOM	404	CG2	ILE	58	2.703	2.311	19.326	1.00	20.39
ATOM	405	CG1	ILE	58	0.661	0.937	19.916	1.00	21.01
ATOM	406	CD1	ILE	58	1.368	0.216	21.094	1.00	21.40
ATOM	407	C	ILE	58	1.583	2.907	16.737	1.00	19.99
ATOM	408	O	ILE	58	1.747	4.110	16.888	1.00	19.32
ATOM	409	N	ASN	59	2.092	2.244	15.706	1.00	19.84
ATOM	410	CA	ASN	59	2.883	2.955	14.705	1.00	20.70
ATOM	411	CB	ASN	59	3.358	1.996	13.612	1.00	19.66
ATOM	412	CG	ASN	59	4.803	1.554	13.836	1.00	19.76
ATOM	413	OD1	ASN	59	5.736	2.319	13.609	1.00	21.26
ATOM	414	ND2	ASN	59	4.985	0.321	14.287	1.00	19.87
ATOM	415	C	ASN	59	2.045	4.083	14.048	1.00	21.81
ATOM	416	O	ASN	59	2.567	5.147	13.720	1.00	21.63
ATOM	417	N	LYS	60	0.752	3.836	13.864	1.00	22.44
ATOM	418	CA	LYS	60	-0.118	4.839	13.249	1.00	23.91
ATOM	419	CB	LYS	60	-1.528	4.280	13.027	1.00	24.44

FIG.11B-10

ATOM	420	CG	LYS	60	-1.552	3.237	11.885	1.00	27.44
ATOM	421	CD	LYS	60	-2.997	2.663	11.665	1.00	29.48
ATOM	422	CE	LYS	60	-4.024	3.744	11.233	1.00	30.95
ATOM	423	NZ	LYS	60	-5.377	3.169	10.933	1.00	32.88
ATOM	424	C	LYS	60	-0.251	6.101	14.078	1.00	24.30
ATOM	425	O	LYS	60	-0.657	7.145	13.574	1.00	24.07
ATOM	426	N	MET	61	0.104	6.012	15.354	1.00	24.01
ATOM	427	CA	MET	61	-0.002	7.157	16.244	1.00	25.12
ATOM	428	CB	MET	61	-0.249	6.693	17.676	1.00	25.40
ATOM	429	CG	MET	61	-1.470	5.835	17.988	1.00	26.45
ATOM	430	SD	MET	61	-1.392	5.217	19.669	1.00	29.36
ATOM	431	CE	MET	61	-1.535	6.797	20.599	1.00	28.93
ATOM	432	C	MET	61	1.255	8.008	16.297	1.00	24.94
ATOM	433	O	MET	61	1.218	9.153	16.749	1.00	26.47
ATOM	434	N	LEU	62	2.359	7.458	15.809	1.00	24.38
ATOM	435	CA	LEU	62	3.651	8.133	15.886	1.00	24.10
ATOM	436	CB	LEU	62	4.742	7.099	16.141	1.00	24.29
ATOM	437	CG	LEU	62	4.251	6.128	17.219	1.00	24.77
ATOM	438	CD1	LEU	62	5.273	5.004	17.283	1.00	24.61
ATOM	439	CD2	LEU	62	4.088	6.800	18.578	1.00	24.56
ATOM	440	C	LEU	62	4.141	8.977	14.723	1.00	23.68
ATOM	441	O	LEU	62	3.965	8.615	13.556	1.00	23.81
ATOM	442	N	ASN	63	4.783	10.095	15.062	1.00	22.77
ATOM	443	CA	ASN	63	5.365	11.007	14.084	1.00	22.30
ATOM	444	CB	ASN	63	4.255	11.825	13.407	1.00	24.66
ATOM	445	CG	ASN	63	4.808	12.770	12.364	1.00	26.67
ATOM	446	OD1	ASN	63	5.808	12.479	11.719	1.00	28.66
ATOM	447	ND2	ASN	63	4.140	13.905	12.177	1.00	28.45
ATOM	448	C	ASN	63	6.385	11.897	14.801	1.00	20.27
ATOM	449	O	ASN	63	6.037	12.930	15.363	1.00	19.93
ATOM	450	N	HIS	64	7.645	11.472	14.795	1.00	18.13
ATOM	451	CA	HIS	64	8.696	12.228	15.459	1.00	17.11
ATOM	452	CB	HIS	64	8.666	11.908	16.960	1.00	16.62
ATOM	453	CG	HIS	64	9.600	12.744	17.769	1.00	15.90
ATOM	454	CD2	HIS	64	9.402	13.904	18.439	1.00	15.85
ATOM	455	ND1	HIS	64	10.934	12.438	17.917	1.00	16.76
ATOM	456	CE1	HIS	64	11.519	13.373	18.642	1.00	16.09
ATOM	457	NE2	HIS	64	10.611	14.275	18.971	1.00	15.69
ATOM	458	C	HIS	64	10.038	11.910	14.827	1.00	17.07
ATOM	459	O	HIS	64	10.278	10.781	14.397	1.00	16.68
ATOM	460	N	GLU	65	10.918	12.908	14.771	1.00	16.86
ATOM	461	CA	GLU	65	12.227	12.746	14.142	1.00	17.23

FIG.11B-11

ATOM	462	CB	GLU	65	12.977	14.081	14.097	1.00	19.17
ATOM	463	CG	GLU	65	13.115	14.589	15.530	1.00	23.09
ATOM	464	CD	GLU	65	12.010	15.573	15.921	1.00	24.78
ATOM	465	OE1	GLU	65	10.804	15.418	15.625	1.00	26.63
ATOM	466	OE2	GLU	65	12.412	16.555	16.575	1.00	29.13
ATOM	467	C	GLU	65	13.165	11.705	14.764	1.00	16.61
ATOM	468	O	GLU	65	14.136	11.290	14.123	1.00	15.95
ATOM	469	N	ASN	66	12.881	11.287	15.999	1.00	15.86
ATOM	470	CA	ASN	66	13.718	10.276	16.645	1.00	15.10
ATOM	471	CB	ASN	66	14.251	10.768	17.999	1.00	14.82
ATOM	472	CG	ASN	66	15.223	11.978	17.803	1.00	14.88
ATOM	473	OD1	ASN	66	14.921	13.102	18.214	1.00	15.31
ATOM	474	ND2	ASN	66	16.373	11.732	17.171	1.00	14.43
ATOM	475	C	ASN	66	12.968	8.975	16.839	1.00	15.46
ATOM	476	O	ASN	66	13.285	8.192	17.740	1.00	14.42
ATOM	477	N	VAL	67	11.976	8.742	15.980	1.00	15.06
ATOM	478	CA	VAL	67	11.188	7.519	16.015	1.00	14.66
ATOM	479	CB	VAL	67	9.752	7.773	16.576	1.00	14.46
ATOM	480	CG1	VAL	67	8.896	6.527	16.418	1.00	14.49
ATOM	481	CG2	VAL	67	9.817	8.155	18.064	1.00	14.92
ATOM	482	C	VAL	67	11.079	7.032	14.567	1.00	15.45
ATOM	483	O	VAL	67	10.730	7.812	13.682	1.00	15.32
ATOM	484	N	VAL	68	11.398	5.762	14.326	1.00	14.74
ATOM	485	CA	VAL	68	11.318	5.209	12.968	1.00	14.94
ATOM	486	CB	VAL	68	11.621	3.688	12.985	1.00	14.98
ATOM	487	CG1	VAL	68	11.344	3.072	11.604	1.00	15.35
ATOM	488	CG2	VAL	68	13.087	3.466	13.331	1.00	13.74
ATOM	489	C	VAL	68	9.953	5.508	12.374	1.00	16.26
ATOM	490	O	VAL	68	8.932	5.061	12.890	1.00	16.70
ATOM	491	N	LYS	69	9.939	6.255	11.272	1.00	17.50
ATOM	492	CA	LYS	69	8.688	6.638	10.629	1.00	20.22
ATOM	493	CB	LYS	69	8.948	7.640	9.496	1.00	22.64
ATOM	494	CG	LYS	69	9.172	9.162	9.649	1.00	26.66
ATOM	495	CD	LYS	69	10.454	9.843	10.196	1.00	29.16
ATOM	496	CE	LYS	69	10.263	11.379	10.284	1.00	29.24
ATOM	497	NZ	LYS	69	11.485	12.071	10.783	1.00	31.62
ATOM	498	C	LYS	69	7.927	5.460	10.056	1.00	20.86
ATOM	499	O	LYS	69	8.526	4.540	9.506	1.00	19.95
ATOM	500	N	PHE	70	6.605	5.497	10.204	1.00	21.61
ATOM	501	CA	PHE	70	5.708	4.465	9.696	1.00	22.90
ATOM	502	CB	PHE	70	4.624	4.154	10.731	1.00	23.86
ATOM	503	CG	PHE	70	3.610	3.142	10.275	1.00	25.07

FIG.11B-12

ATOM	504	CD1	PHE	70	3.984	1.828	10.020	1.00	25.78
ATOM	505	CD2	PHE	70	2.272	3.496	10.149	1.00	25.74
ATOM	506	CE1	PHE	70	3.038	0.873	9.652	1.00	27.17
ATOM	507	CE2	PHE	70	1.310	2.547	9.780	1.00	26.29
ATOM	508	CZ	PHE	70	1.695	1.237	9.534	1.00	26.19
ATOM	509	C	PHE	70	5.020	5.030	8.425	1.00	23.33
ATOM	510	O	PHE	70	4.312	6.038	8.492	1.00	22.78
ATOM	511	N	TYR	71	5.226	4.372	7.291	1.00	24.38
ATOM	512	CA	TYR	71	4.639	4.836	6.037	1.00	26.22
ATOM	513	CB	TYR	71	5.615	4.622	4.886	1.00	25.69
ATOM	514	CG	TYR	71	6.947	5.313	5.058	1.00	25.34
ATOM	515	CD1	TYR	71	7.023	6.687	5.293	1.00	25.68
ATOM	516	CE1	TYR	71	8.263	7.337	5.366	1.00	25.78
ATOM	517	CD2	TYR	71	8.139	4.606	4.910	1.00	25.28
ATOM	518	CE2	TYR	71	9.372	5.243	4.982	1.00	25.14
ATOM	519	CZ	TYR	71	9.427	6.608	5.204	1.00	25.13
ATOM	520	OH	TYR	71	10.653	7.239	5.223	1.00	26.09
ATOM	521	C	TYR	71	3.327	4.161	5.657	1.00	27.64
ATOM	522	O	TYR	71	2.579	4.675	4.817	1.00	28.91
ATOM	523	N	GLY	72	3.044	3.016	6.269	1.00	28.78
ATOM	524	CA	GLY	72	1.814	2.306	5.967	1.00	30.86
ATOM	525	C	GLY	72	1.968	0.802	6.067	1.00	31.92
ATOM	526	O	GLY	72	3.057	0.297	6.326	1.00	31.91
ATOM	527	N	HIS	73	0.872	0.080	5.862	1.00	33.79
ATOM	528	CA	HIS	73	0.900	-1.376	5.932	1.00	35.69
ATOM	529	CB	HIS	73	0.508	-1.844	7.333	1.00	35.93
ATOM	530	CG	HIS	73	-0.894	-1.487	7.718	1.00	35.89
ATOM	531	CD2	HIS	73	-1.460	-0.295	8.022	1.00	36.24
ATOM	532	ND1	HIS	73	-1.900	-2.424	7.814	1.00	35.93
ATOM	533	CE1	HIS	73	-3.025	-1.825	8.163	1.00	36.12
ATOM	534	NE2	HIS	73	-2.785	-0.533	8.296	1.00	36.36
ATOM	535	C	HIS	73	-0.058	-1.992	4.924	1.00	37.26
ATOM	536	O	HIS	73	-1.020	-1.351	4.503	1.00	37.54
ATOM	537	N	ARG	74	0.215	-3.236	4.542	1.00	39.37
ATOM	538	CA	ARG	74	-0.617	-3.957	3.582	1.00	41.57
ATOM	539	CB	ARG	74	0.193	-4.335	2.342	1.00	42.35
ATOM	540	CG	ARG	74	0.662	-3.169	1.465	1.00	43.17
ATOM	541	CD	ARG	74	1.492	-3.729	0.290	1.00	43.98
ATOM	542	NE	ARG	74	0.755	-4.738	-0.469	1.00	44.77
ATOM	543	CZ	ARG	74	1.259	-5.412	-1.497	1.00	44.92
ATOM	544	NH1	ARG	74	2.505	-5.184	-1.892	1.00	45.32
ATOM	545	NH2	ARG	74	0.523	-6.320	-2.126	1.00	45.08

FIG.11B-13

ATOM	546	C	ARG	74	-1.194	-5.241	4.175	1.00	42.67
ATOM	547	O	ARG	74	-0.714	-5.738	5.196	1.00	43.41
ATOM	548	N	ARG	75	-2.219	-5.773	3.513	1.00	43.71
ATOM	549	CA	ARG	75	-2.904	-6.993	3.945	1.00	44.56
ATOM	550	CB	ARG	75	-4.356	-6.992	3.455	1.00	44.64
ATOM	551	CG	ARG	75	-5.231	-5.765	3.791	1.00	45.27
ATOM	552	CD	ARG	75	-5.688	-5.646	5.256	1.00	45.40
ATOM	553	NE	ARG	75	-6.632	-6.700	5.620	1.00	45.56
ATOM	554	CZ	ARG	75	-7.160	-6.844	6.831	1.00	45.42
ATOM	555	NH1	ARG	75	-6.835	-6.002	7.804	1.00	45.59
ATOM	556	NH2	ARG	75	-8.021	-7.825	7.071	1.00	45.46
ATOM	557	C	ARG	75	-2.253	-8.266	3.377	1.00	44.76
ATOM	558	O	ARG	75	-1.782	-9.124	4.124	1.00	45.26
ATOM	559	N	GLU	76	-2.247	-8.370	2.052	1.00	44.88
ATOM	560	CA	GLU	76	-1.680	-9.517	1.346	1.00	44.86
ATOM	561	CB	GLU	76	-0.152	-9.439	1.337	1.00	45.21
ATOM	562	CG	GLU	76	0.450	-10.469	0.334	1.00	45.31
ATOM	563	CD	GLU	76	0.050	-10.137	-1.107	1.00	45.52
ATOM	564	OE1	GLU	76	0.511	-9.104	-1.639	1.00	45.49
ATOM	565	OE2	GLU	76	-0.731	-10.912	-1.704	1.00	45.23
ATOM	566	C	GLU	76	-2.116	-10.859	1.960	1.00	44.61
ATOM	567	O	GLU	76	-1.297	-11.758	2.171	1.00	44.52
ATOM	568	N	GLY	77	-3.409	-10.977	2.247	1.00	44.26
ATOM	569	CA	GLY	77	-3.938	-12.204	2.819	1.00	43.80
ATOM	570	C	GLY	77	-3.414	-12.551	4.202	1.00	43.49
ATOM	571	O	GLY	77	-3.923	-12.054	5.208	1.00	43.67
ATOM	572	N	ASN	78	-2.402	-13.415	4.251	1.00	43.27
ATOM	573	CA	ASN	78	-1.809	-13.841	5.517	1.00	43.15
ATOM	574	CB	ASN	78	-1.743	-15.371	5.593	1.00	43.84
ATOM	575	CG	ASN	78	-3.146	-15.993	5.490	1.00	44.43
ATOM	576	OD1	ASN	78	-3.797	-15.925	4.444	1.00	44.43
ATOM	577	ND2	ASN	78	-3.608	-16.593	6.583	1.00	44.71
ATOM	578	C	ASN	78	-0.382	-13.285	5.753	1.00	42.53
ATOM	579	O	ASN	78	0.299	-13.684	6.699	1.00	43.03
ATOM	580	N	ILE	79	0.061	-12.378	4.888	1.00	41.52
ATOM	581	CA	ILE	79	1.387	-11.782	5.035	1.00	40.34
ATOM	582	CB	ILE	79	2.264	-12.027	3.778	1.00	40.55
ATOM	583	CG2	ILE	79	3.645	-11.411	3.973	1.00	40.53
ATOM	584	CG1	ILE	79	2.415	-13.530	3.519	1.00	40.50
ATOM	585	CD1	ILE	79	3.142	-14.304	4.645	1.00	40.17
ATOM	586	C	ILE	79	1.243	-10.281	5.242	1.00	39.50
ATOM	587	O	ILE	79	0.747	-9.578	4.362	1.00	39.47

FIG.11B-14

ATOM	588	N	GLN	80	1.658	-9.794	6.411	1.00	38.59
ATOM	589	CA	GLN	80	1.584	-8.368	6.729	1.00	37.48
ATOM	590	CB	GLN	80	1.413	-8.135	8.237	1.00	38.53
ATOM	591	CG	GLN	80	0.116	-8.469	8.997	1.00	39.05
ATOM	592	CD	GLN	80	-1.025	-7.622	8.446	1.00	39.69
ATOM	593	OE1	GLN	80	-0.923	-6.397	8.363	1.00	40.14
ATOM	594	NE2	GLN	80	-2.119	-8.277	8.069	1.00	39.68
ATOM	595	C	GLN	80	2.865	-7.668	6.312	1.00	36.30
ATOM	596	O	GLN	80	3.963	-8.158	6.570	1.00	36.40
ATOM	597	N	TYR	81	2.721	-6.518	5.662	1.00	34.84
ATOM	598	CA	TYR	81	3.870	-5.741	5.194	1.00	33.41
ATOM	599	CB	TYR	81	3.809	-5.546	3.674	1.00	33.77
ATOM	600	CG	TYR	81	4.000	-6.809	2.856	1.00	34.37
ATOM	601	CD1	TYR	81	5.272	-7.243	2.492	1.00	34.27
ATOM	602	CE1	TYR	81	5.452	-8.406	1.740	1.00	34.76
ATOM	603	CD2	TYR	81	2.903	-7.571	2.450	1.00	34.73
ATOM	604	CE2	TYR	81	3.074	-8.735	1.701	1.00	34.90
ATOM	605	CZ	TYR	81	4.349	-9.145	1.350	1.00	34.65
ATOM	606	OH	TYR	81	4.517	-10.296	0.614	1.00	35.49
ATOM	607	C	TYR	81	3.873	-4.343	5.834	1.00	31.88
ATOM	608	O	TYR	81	2.965	-3.548	5.602	1.00	32.17
ATOM	609	N	LEU	82	4.893	-4.048	6.636	1.00	29.86
ATOM	610	CA	LEU	82	4.985	-2.738	7.272	1.00	28.10
ATOM	611	CB	LEU	82	5.310	-2.871	8.769	1.00	28.19
ATOM	612	CG	LEU	82	4.240	-3.477	9.686	1.00	29.26
ATOM	613	CD1	LEU	82	4.674	-3.203	11.133	1.00	28.77
ATOM	614	CD2	LEU	82	2.873	-2.867	9.431	1.00	29.93
ATOM	615	C	LEU	82	6.083	-1.916	6.606	1.00	26.82
ATOM	616	O	LEU	82	7.241	-2.326	6.582	1.00	26.42
ATOM	617	N	PHE	83	5.711	-0.765	6.054	1.00	25.82
ATOM	618	CA	PHE	83	6.673	0.106	5.387	1.00	24.50
ATOM	619	CB	PHE	83	6.008	0.772	4.180	1.00	25.77
ATOM	620	CG	PHE	83	5.548	-0.209	3.142	1.00	27.12
ATOM	621	CD1	PHE	83	4.377	-0.942	3.324	1.00	28.41
ATOM	622	CD2	PHE	83	6.322	-0.447	2.013	1.00	28.63
ATOM	623	CE1	PHE	83	3.984	-1.908	2.389	1.00	29.75
ATOM	624	CE2	PHE	83	5.941	-1.408	1.074	1.00	29.85
ATOM	625	CZ	PHE	83	4.769	-2.140	1.268	1.00	29.73
ATOM	626	C	PHE	83	7.185	1.100	6.382	1.00	23.00
ATOM	627	O	PHE	83	6.427	1.908	6.910	1.00	22.13
ATOM	628	N	LEU	84	8.492	1.044	6.628	1.00	21.28
ATOM	629	CA	LEU	84	9.144	1.901	7.616	1.00	20.54

FIG.11B-15

ATOM	630	CB	LEU	84	9.713	1.040	8.745	1.00	19.57
ATOM	631	CG	LEU	84	8.713	0.013	9.290	1.00	18.62
ATOM	632	CD1	LEU	84	9.495	-1.049	10.055	1.00	19.29
ATOM	633	CD2	LEU	84	7.671	0.657	10.175	1.00	19.74
ATOM	634	C	LEU	84	10.331	2.710	7.085	1.00	20.28
ATOM	635	O	LEU	84	10.912	2.396	6.041	1.00	20.78
ATOM	636	N	GLU	85	10.691	3.746	7.834	1.00	19.73
ATOM	637	CA	GLU	85	11.828	4.596	7.502	1.00	19.25
ATOM	638	CB	GLU	85	11.983	5.690	8.563	1.00	19.19
ATOM	639	CG	GLU	85	13.227	6.565	8.390	1.00	19.69
ATOM	640	CD	GLU	85	13.164	7.676	9.440	1.00	20.12
ATOM	641	OE1	GLU	85	13.955	8.637	9.305	1.00	20.13
ATOM	642	OE2	GLU	85	12.341	7.578	10.375	1.00	18.21
ATOM	643	C	GLU	85	13.105	3.768	7.474	1.00	19.30
ATOM	644	O	GLU	85	13.454	3.115	8.461	1.00	18.82
ATOM	645	N	TYR	86	13.806	3.775	6.346	1.00	18.76
ATOM	646	CA	TYR	86	15.037	3.021	6.249	1.00	18.51
ATOM	647	CB	TYR	86	15.406	2.799	4.782	1.00	19.67
ATOM	648	CG	TYR	86	16.774	2.195	4.610	1.00	20.99
ATOM	649	CD1	TYR	86	17.106	0.992	5.233	1.00	21.68
ATOM	650	CE1	TYR	86	18.372	0.434	5.091	1.00	22.49
ATOM	651	CD2	TYR	86	17.747	2.827	3.829	1.00	21.14
ATOM	652	CE2	TYR	86	19.019	2.272	3.682	1.00	22.21
ATOM	653	CZ	TYR	86	19.321	1.082	4.318	1.00	23.27
ATOM	654	OH	TYR	86	20.585	0.548	4.216	1.00	25.97
ATOM	655	C	TYR	86	16.167	3.769	6.953	1.00	18.53
ATOM	656	O	TYR	86	16.444	4.927	6.631	1.00	17.92
ATOM	657	N	CYS	87	16.797	3.110	7.926	1.00	18.60
ATOM	658	CA	CYS	87	17.904	3.705	8.678	1.00	19.08
ATOM	659	CB	CYS	87	17.697	3.474	10.187	1.00	18.77
ATOM	660	SG	CYS	87	16.171	4.310	10.710	1.00	18.39
ATOM	661	C	CYS	87	19.193	3.058	8.186	1.00	18.78
ATOM	662	O	CYS	87	19.571	1.968	8.626	1.00	19.02
ATOM	663	N	SER	88	19.879	3.739	7.271	1.00	19.59
ATOM	664	CA	SER	88	21.098	3.200	6.687	1.00	20.13
ATOM	665	CB	SER	88	21.508	4.021	5.458	1.00	20.76
ATOM	666	OG	SER	88	21.898	5.331	5.835	1.00	21.97
ATOM	667	C	SER	88	22.308	3.098	7.584	1.00	20.67
ATOM	668	O	SER	88	23.273	2.419	7.240	1.00	21.00
ATOM	669	N	GLY	89	22.263	3.758	8.739	1.00	20.40
ATOM	670	CA	GLY	89	23.392	3.718	9.648	1.00	20.92
ATOM	671	C	GLY	89	23.476	2.498	10.544	1.00	20.54

FIG.11B-16

ATOM	672	O	GLY	89	24.443	2.343	11.285	1.00	21.32
ATOM	673	N	GLY	90	22.465	1.636	10.497	1.00	20.52
ATOM	674	CA	GLY	90	22.495	0.435	11.308	1.00	20.74
ATOM	675	C	GLY	90	22.057	0.669	12.739	1.00	19.72
ATOM	676	O	GLY	90	21.393	1.653	13.041	1.00	19.15
ATOM	677	N	GLU	91	22.454	-0.243	13.618	1.00	19.25
ATOM	678	CA	GLU	91	22.095	-0.175	15.032	1.00	18.39
ATOM	679	CB	GLU	91	21.985	-1.580	15.616	1.00	19.43
ATOM	680	CG	GLU	91	20.935	-2.428	14.909	1.00	20.97
ATOM	681	CD	GLU	91	20.884	-3.864	15.432	1.00	21.99
ATOM	682	OE1	GLU	91	20.081	-4.642	14.863	1.00	23.57
ATOM	683	OE2	GLU	91	21.624	-4.182	16.387	1.00	20.79
ATOM	684	C	GLU	91	23.102	0.554	15.861	1.00	17.51
ATOM	685	O	GLU	91	24.289	0.558	15.549	1.00	18.50
ATOM	686	N	LEU	92	22.628	1.188	16.931	1.00	16.35
ATOM	687	CA	LEU	92	23.507	1.908	17.845	1.00	16.25
ATOM	688	CB	LEU	92	22.684	2.598	18.945	1.00	15.21
ATOM	689	CG	LEU	92	23.525	3.275	20.041	1.00	13.57
ATOM	690	CD1	LEU	92	24.312	4.465	19.512	1.00	14.82
ATOM	691	CD2	LEU	92	22.545	3.710	21.139	1.00	14.32
ATOM	692	C	LEU	92	24.417	0.890	18.448	1.00	17.07
ATOM	693	O	LEU	92	25.559	1.185	18.784	1.00	16.10
ATOM	694	N	PHE	93	23.918	-0.342	18.552	1.00	17.48
ATOM	695	CA	PHE	93	24.678	-1.438	19.121	1.00	20.02
ATOM	696	CB	PHE	93	23.888	-2.751	18.999	1.00	21.58
ATOM	697	CG	PHE	93	24.629	-3.956	19.521	1.00	23.36
ATOM	698	CD1	PHE	93	25.553	-4.628	18.721	1.00	23.91
ATOM	699	CD2	PHE	93	24.420	-4.402	20.822	1.00	24.46
ATOM	700	CE1	PHE	93	26.261	-5.730	19.212	1.00	25.32
ATOM	701	CE2	PHE	93	25.124	-5.506	21.328	1.00	25.27
ATOM	702	CZ	PHE	93	26.045	-6.168	20.522	1.00	24.89
ATOM	703	C	PHE	93	26.039	-1.606	18.425	1.00	21.14
ATOM	704	O	PHE	93	27.050	-1.856	19.082	1.00	20.61
ATOM	705	N	ASP	94	26.051	-1.450	17.104	1.00	21.54
ATOM	706	CA	ASP	94	27.277	-1.614	16.318	1.00	22.83
ATOM	707	CB	ASP	94	26.908	-1.933	14.857	1.00	24.16
ATOM	708	CG	ASP	94	26.277	-3.346	14.811	1.00	25.84
ATOM	709	OD1	ASP	94	25.502	-3.688	13.893	1.00	29.46
ATOM	710	OD2	ASP	94	26.543	-4.189	15.686	1.00	26.49
ATOM	711	C	ASP	94	28.249	-0.425	16.407	1.00	22.49
ATOM	712	O	ASP	94	29.365	-0.497	15.896	1.00	23.70
ATOM	713	N	ARG	95	27.839	0.645	17.084	1.00	21.43

FIG.11B-17

ATOM	714	CA	ARG	95	28.685	1.826	17.250	1.00	20.91
ATOM	715	CB	ARG	95	27.837	3.099	17.129	1.00	23.48
ATOM	716	CG	ARG	95	27.411	3.256	15.674	1.00	26.51
ATOM	717	CD	ARG	95	28.661	3.755	14.919	1.00	28.94
ATOM	718	NE	ARG	95	29.128	5.018	15.492	1.00	32.20
ATOM	719	CZ	ARG	95	28.577	6.203	15.239	1.00	33.03
ATOM	720	NH1	ARG	95	27.544	6.292	14.407	1.00	35.34
ATOM	721	NH2	ARG	95	29.038	7.291	15.836	1.00	33.60
ATOM	722	C	ARG	95	29.378	1.815	18.636	1.00	20.22
ATOM	723	O	ARG	95	30.171	2.706	18.957	1.00	20.16
ATOM	724	N	ILE	96	29.051	0.802	19.435	1.00	19.47
ATOM	725	CA	ILE	96	29.605	0.640	20.771	1.00	18.75
ATOM	726	CB	ILE	96	28.532	0.091	21.721	1.00	18.34
ATOM	727	CG2	ILE	96	29.123	-0.162	23.104	1.00	18.88
ATOM	728	CG1	ILE	96	27.371	1.085	21.777	1.00	17.58
ATOM	729	CD1	ILE	96	26.167	0.580	22.596	1.00	16.35
ATOM	730	C	ILE	96	30.775	-0.298	20.702	1.00	19.98
ATOM	731	O	ILE	96	30.609	-1.486	20.427	1.00	19.77
ATOM	732	N	GLU	97	31.968	0.230	20.943	1.00	19.99
ATOM	733	CA	GLU	97	33.168	-0.597	20.886	1.00	22.20
ATOM	734	CB	GLU	97	34.383	0.292	20.633	1.00	24.46
ATOM	735	CG	GLU	97	34.631	1.057	19.276	1.00	28.88
ATOM	736	CD	GLU	97	33.720	2.218	18.832	1.00	31.18
ATOM	737	OE1	GLU	97	33.585	3.250	19.536	1.00	32.29
ATOM	738	OE2	GLU	97	33.142	2.070	17.730	1.00	33.32
ATOM	739	C	GLU	97	33.307	-1.427	22.185	1.00	21.17
ATOM	740	O	GLU	97	33.320	-0.886	23.289	1.00	21.38
ATOM	741	N	PRO	98	33.391	-2.757	22.055	1.00	21.50
ATOM	742	CD	PRO	98	33.282	-3.558	20.817	1.00	21.52
ATOM	743	CA	PRO	98	33.519	-3.622	23.231	1.00	21.75
ATOM	744	CB	PRO	98	33.765	-4.998	22.611	1.00	21.99
ATOM	745	CG	PRO	98	32.982	-4.935	21.349	1.00	22.40
ATOM	746	C	PRO	98	34.593	-3.186	24.219	1.00	22.45
ATOM	747	O	PRO	98	35.722	-2.885	23.827	1.00	22.61
ATOM	748	N	ASP	99	34.212	-3.168	25.495	1.00	23.48
ATOM	749	CA	ASP	99	35.072	-2.804	26.616	1.00	24.51
ATOM	750	CB	ASP	99	36.323	-3.695	26.634	1.00	27.46
ATOM	751	CG	ASP	99	36.003	-5.182	26.423	1.00	30.42
ATOM	752	OD1	ASP	99	35.439	-5.526	25.362	1.00	32.42
ATOM	753	OD2	ASP	99	36.309	-6.023	27.298	1.00	32.91
ATOM	754	C	ASP	99	35.524	-1.341	26.625	1.00	23.52
ATOM	755	O	ASP	99	36.266	-0.917	27.512	1.00	23.73

FIG.11B-18

ATOM	756	N	ILE	100	35.082	-0.561	25.650	1.00	22.38
ATOM	757	CA	ILE	100	35.490	0.828	25.594	1.00	21.76
ATOM	758	CB	ILE	100	36.493	1.045	24.440	1.00	23.97
ATOM	759	CG2	ILE	100	37.824	0.408	24.782	1.00	24.47
ATOM	760	CG1	ILE	100	36.017	0.329	23.181	1.00	25.90
ATOM	761	CD1	ILE	100	37.095	0.266	22.055	1.00	28.42
ATOM	762	C	ILE	100	34.351	1.797	25.504	1.00	20.24
ATOM	763	O	ILE	100	34.340	2.797	26.212	1.00	19.97
ATOM	764	N	GLY	101	33.389	1.512	24.637	1.00	18.48
ATOM	765	CA	GLY	101	32.249	2.405	24.481	1.00	16.99
ATOM	766	C	GLY	101	32.418	3.264	23.241	1.00	16.69
ATOM	767	O	GLY	101	32.595	2.739	22.136	1.00	17.27
ATOM	768	N	MET	102	32.324	4.581	23.419	1.00	16.05
ATOM	769	CA	MET	102	32.483	5.546	22.335	1.00	15.12
ATOM	770	CB	MET	102	31.181	5.702	21.541	1.00	15.01
ATOM	771	CG	MET	102	30.080	6.447	22.316	1.00	14.98
ATOM	772	SD	MET	102	28.559	6.611	21.344	1.00	14.69
ATOM	773	CE	MET	102	28.049	4.872	21.224	1.00	14.44
ATOM	774	C	MET	102	32.834	6.921	22.981	1.00	14.62
ATOM	775	O	MET	102	32.713	7.100	24.202	1.00	13.88
ATOM	776	N	PRO	103	33.264	7.894	22.171	1.00	15.17
ATOM	777	CD	PRO	103	33.526	7.844	20.723	1.00	14.81
ATOM	778	CA	PRO	103	33.609	9.213	22.715	1.00	14.86
ATOM	779	CB	PRO	103	33.984	10.003	21.459	1.00	15.81
ATOM	780	CG	PRO	103	34.530	8.944	20.559	1.00	16.07
ATOM	781	C	PRO	103	32.435	9.812	23.479	1.00	15.44
ATOM	782	O	PRO	103	31.308	9.789	22.994	1.00	14.56
ATOM	783	N	GLU	104	32.701	10.351	24.664	1.00	15.05
ATOM	784	CA	GLU	104	31.646	10.948	25.484	1.00	15.48
ATOM	785	CB	GLU	104	32.263	11.608	26.727	1.00	16.12
ATOM	786	CG	GLU	104	31.299	11.754	27.906	1.00	15.88
ATOM	787	CD	GLU	104	32.003	12.243	29.171	1.00	17.77
ATOM	788	OE1	GLU	104	31.686	13.387	29.576	1.00	17.94
ATOM	789	OE2	GLU	104	32.848	11.498	29.737	1.00	17.72
ATOM	790	C	GLU	104	30.748	11.959	24.731	1.00	16.01
ATOM	791	O	GLU	104	29.533	11.998	24.960	1.00	15.90
ATOM	792	N	PRO	105	31.324	12.790	23.840	1.00	16.31
ATOM	793	CD	PRO	105	32.740	13.149	23.642	1.00	17.39
ATOM	794	CA	PRO	105	30.442	13.732	23.140	1.00	16.34
ATOM	795	CB	PRO	105	31.427	14.609	22.360	1.00	17.22
ATOM	796	CG	PRO	105	32.645	14.618	23.260	1.00	17.15
ATOM	797	C	PRO	105	29.418	12.999	22.282	1.00	15.69

FIG.11B-19

ATOM	798	O	PRO	105	28.262	13.414	22.179	1.00	15.94
ATOM	799	N	ASP	106	29.846	11.913	21.651	1.00	15.00
ATOM	800	CA	ASP	106	28.946	11.142	20.810	1.00	15.05
ATOM	801	CB	ASP	106	29.695	10.033	20.070	1.00	17.35
ATOM	802	CG	ASP	106	30.678	10.536	19.027	1.00	20.16
ATOM	803	OD1	ASP	106	30.627	11.731	18.686	1.00	23.79
ATOM	804	OD2	ASP	106	31.495	9.725	18.541	1.00	24.67
ATOM	805	C	ASP	106	27.863	10.473	21.654	1.00	14.46
ATOM	806	O	ASP	106	26.696	10.403	21.240	1.00	13.76
ATOM	807	N	ALA	107	28.249	9.956	22.816	1.00	13.14
ATOM	808	CA	ALA	107	27.284	9.307	23.692	1.00	12.29
ATOM	809	CB	ALA	107	27.990	8.674	24.900	1.00	11.81
ATOM	810	C	ALA	107	26.256	10.368	24.177	1.00	12.80
ATOM	811	O	ALA	107	25.065	10.098	24.262	1.00	11.19
ATOM	812	N	GLN	108	26.735	11.571	24.478	1.00	12.72
ATOM	813	CA	GLN	108	25.838	12.620	24.964	1.00	13.51
ATOM	814	CB	GLN	108	26.648	13.839	25.395	1.00	13.39
ATOM	815	CG	GLN	108	25.730	14.775	26.208	1.00	13.91
ATOM	816	CD	GLN	108	26.315	16.169	26.290	1.00	14.73
ATOM	817	OE1	GLN	108	26.409	16.750	27.380	1.00	18.02
ATOM	818	NE2	GLN	108	26.690	16.726	25.142	1.00	13.66
ATOM	819	C	GLN	108	24.828	13.007	23.886	1.00	12.49
ATOM	820	O	GLN	108	23.643	13.184	24.163	1.00	12.86
ATOM	821	N	ARG	109	25.298	13.139	22.652	1.00	12.91
ATOM	822	CA	ARG	109	24.412	13.495	21.544	1.00	12.93
ATOM	823	CB	ARG	109	25.242	13.672	20.270	1.00	15.25
ATOM	824	CG	ARG	109	24.424	13.899	18.967	1.00	17.36
ATOM	825	CD	ARG	109	25.431	14.120	17.816	1.00	20.06
ATOM	826	NE	ARG	109	26.088	12.870	17.433	1.00	25.24
ATOM	827	CZ	ARG	109	25.498	11.902	16.732	1.00	25.26
ATOM	828	NH1	ARG	109	24.251	12.039	16.331	1.00	24.49
ATOM	829	NH2	ARG	109	26.157	10.787	16.442	1.00	29.46
ATOM	830	C	ARG	109	23.334	12.421	21.342	1.00	12.86
ATOM	831	O	ARG	109	22.153	12.739	21.192	1.00	12.23
ATOM	832	N	PHE	110	23.742	11.154	21.345	1.00	11.06
ATOM	833	CA	PHE	110	22.778	10.075	21.174	1.00	11.02
ATOM	834	CB	PHE	110	23.453	8.706	21.090	1.00	11.45
ATOM	835	CG	PHE	110	24.187	8.462	19.801	1.00	12.74
ATOM	836	CD1	PHE	110	23.586	8.730	18.567	1.00	12.74
ATOM	837	CD2	PHE	110	25.470	7.916	19.822	1.00	12.74
ATOM	838	CE1	PHE	110	24.255	8.453	17.360	1.00	13.26
ATOM	839	CE2	PHE	110	26.142	7.633	18.622	1.00	14.73

FIG.11B-20

ATOM	840	CZ	PHE	110	25.539	7.899	17.401	1.00	13.07
ATOM	841	C	PHE	110	21.819	10.031	22.356	1.00	11.04
ATOM	842	O	PHE	110	20.631	9.735	22.192	1.00	10.10
ATOM	843	N	PHE	111	22.325	10.298	23.558	1.00	10.21
ATOM	844	CA	PHE	111	21.455	10.278	24.729	1.00	10.84
ATOM	845	CB	PHE	111	22.279	10.392	26.022	1.00	10.93
ATOM	846	CG	PHE	111	21.483	10.099	27.265	1.00	11.01
ATOM	847	CD1	PHE	111	21.091	8.793	27.569	1.00	10.73
ATOM	848	CD2	PHE	111	21.087	11.137	28.111	1.00	11.89
ATOM	849	CE1	PHE	111	20.298	8.528	28.710	1.00	12.71
ATOM	850	CE2	PHE	111	20.307	10.888	29.235	1.00	12.60
ATOM	851	CZ	PHE	111	19.907	9.581	29.536	1.00	12.53
ATOM	852	C	PHE	111	20.423	11.414	24.651	1.00	10.82
ATOM	853	O	PHE	111	19.276	11.251	25.049	1.00	10.73
ATOM	854	N	HIS	112	20.834	12.560	24.125	1.00	11.50
ATOM	855	CA	HIS	112	19.908	13.678	23.986	1.00	12.31
ATOM	856	CB	HIS	112	20.562	14.893	23.322	1.00	12.79
ATOM	857	CG	HIS	112	21.594	15.584	24.158	1.00	14.79
ATOM	858	CD2	HIS	112	22.655	16.344	23.797	1.00	14.31
ATOM	859	ND1	HIS	112	21.544	15.626	25.534	1.00	15.64
ATOM	860	CE1	HIS	112	22.523	16.389	25.987	1.00	12.99
ATOM	861	NE2	HIS	112	23.212	16.838	24.951	1.00	17.59
ATOM	862	C	HIS	112	18.788	13.282	23.019	1.00	12.56
ATOM	863	O	HIS	112	17.608	13.540	23.278	1.00	13.20
ATOM	864	N	GLN	113	19.179	12.659	21.906	1.00	12.60
ATOM	865	CA	GLN	113	18.226	12.236	20.881	1.00	12.31
ATOM	866	CB	GLN	113	18.967	11.756	19.622	1.00	12.91
ATOM	867	CG	GLN	113	19.661	12.997	18.985	1.00	13.65
ATOM	868	CD	GLN	113	20.372	12.578	17.695	1.00	17.58
ATOM	869	OE1	GLN	113	20.322	11.416	17.302	1.00	20.92
ATOM	870	NE2	GLN	113	21.037	13.530	17.037	1.00	17.64
ATOM	871	C	GLN	113	17.338	11.160	21.406	1.00	12.18
ATOM	872	O	GLN	113	16.142	11.132	21.113	1.00	12.09
ATOM	873	N	LEU	114	17.906	10.267	22.209	1.00	10.60
ATOM	874	CA	LEU	114	17.116	9.188	22.804	1.00	10.15
ATOM	875	CB	LEU	114	18.024	8.262	23.621	1.00	9.54
ATOM	876	CG	LEU	114	17.324	7.170	24.451	1.00	10.18
ATOM	877	CD1	LEU	114	16.473	6.276	23.565	1.00	9.65
ATOM	878	CD2	LEU	114	18.382	6.296	25.143	1.00	8.88
ATOM	879	C	LEU	114	16.043	9.818	23.754	1.00	9.97
ATOM	880	O	LEU	114	14.863	9.448	23.725	1.00	9.93
ATOM	881	N	MET	115	16.455	10.763	24.589	1.00	9.92

FIG.11B-21

ATOM	882	CA	MET	115	15.485	11.403	25.489	1.00	11.27
ATOM	883	CB	MET	115	16.162	12.439	26.386	1.00	12.20
ATOM	884	CG	MET	115	17.001	11.884	27.520	1.00	12.71
ATOM	885	SD	MET	115	16.069	10.850	28.678	1.00	15.32
ATOM	886	CE	MET	115	16.509	9.262	27.927	1.00	10.45
ATOM	887	C	MET	115	14.379	12.124	24.719	1.00	11.42
ATOM	888	O	MET	115	13.218	12.126	25.129	1.00	12.59
ATOM	889	N	ALA	116	14.741	12.739	23.599	1.00	12.11
ATOM	890	CA	ALA	116	13.762	13.454	22.785	1.00	11.80
ATOM	891	CB	ALA	116	14.458	14.124	21.613	1.00	12.68
ATOM	892	C	ALA	116	12.697	12.456	22.290	1.00	12.52
ATOM	893	O	ALA	116	11.496	12.737	22.347	1.00	12.58
ATOM	894	N	GLY	117	13.153	11.299	21.818	1.00	10.70
ATOM	895	CA	GLY	117	12.236	10.276	21.338	1.00	11.42
ATOM	896	C	GLY	117	11.375	9.700	22.446	1.00	11.35
ATOM	897	O	GLY	117	10.176	9.490	22.267	1.00	11.68
ATOM	898	N	VAL	118	11.976	9.441	23.606	1.00	11.46
ATOM	899	CA	VAL	118	11.221	8.877	24.721	1.00	10.70
ATOM	900	CB	VAL	118	12.191	8.367	25.805	1.00	10.80
ATOM	901	CG1	VAL	118	11.423	7.893	27.032	1.00	11.15
ATOM	902	CG2	VAL	118	13.005	7.230	25.232	1.00	10.87
ATOM	903	C	VAL	118	10.199	9.886	25.280	1.00	11.94
ATOM	904	O	VAL	118	9.043	9.514	25.567	1.00	12.27
ATOM	905	N	VAL	119	10.619	11.143	25.428	1.00	11.92
ATOM	906	CA	VAL	119	9.718	12.200	25.898	1.00	13.60
ATOM	907	CB	VAL	119	10.376	13.614	25.844	1.00	14.14
ATOM	908	CG1	VAL	119	9.310	14.696	25.990	1.00	14.89
ATOM	909	CG2	VAL	119	11.385	13.763	26.972	1.00	14.60
ATOM	910	C	VAL	119	8.506	12.256	24.966	1.00	13.79
ATOM	911	O	VAL	119	7.355	12.380	25.405	1.00	14.60
ATOM	912	N	TYR	120	8.773	12.159	23.669	1.00	13.68
ATOM	913	CA	TYR	120	7.687	12.192	22.696	1.00	13.72
ATOM	914	CB	TYR	120	8.243	12.109	21.286	1.00	14.04
ATOM	915	CG	TYR	120	7.157	11.900	20.273	1.00	15.90
ATOM	916	CD1	TYR	120	6.309	12.949	19.914	1.00	16.61
ATOM	917	CE1	TYR	120	5.250	12.740	19.032	1.00	17.36
ATOM	918	CD2	TYR	120	6.924	10.641	19.732	1.00	16.53
ATOM	919	CE2	TYR	120	5.869	10.421	18.859	1.00	17.32
ATOM	920	CZ	TYR	120	5.038	11.475	18.509	1.00	18.22
ATOM	921	OH	TYR	120	3.998	11.244	17.634	1.00	18.59
ATOM	922	C	TYR	120	6.705	11.001	22.906	1.00	13.65
ATOM	923	O	TYR	120	5.481	11.193	23.015	1.00	13.76

FIG.11B-22

ATOM	924	N	LEU	121	7.245	9.786	22.968	1.00	11.97
ATOM	925	CA	LEU	121	6.407	8.610	23.155	1.00	11.14
ATOM	926	CB	LEU	121	7.262	7.337	23.236	1.00	10.46
ATOM	927	CG	LEU	121	8.001	6.961	21.937	1.00	9.60
ATOM	928	CD1	LEU	121	8.830	5.695	22.199	1.00	12.56
ATOM	929	CD2	LEU	121	7.039	6.749	20.774	1.00	11.38
ATOM	930	C	LEU	121	5.576	8.726	24.452	1.00	11.75
ATOM	931	O	LEU	121	4.373	8.479	24.455	1.00	10.61
ATOM	932	N	HIS	122	6.234	9.089	25.553	1.00	11.66
ATOM	933	CA	HIS	122	5.524	9.194	26.820	1.00	11.84
ATOM	934	CB	HIS	122	6.528	9.447	27.951	1.00	12.54
ATOM	935	CG	HIS	122	7.381	8.255	28.262	1.00	11.35
ATOM	936	CD2	HIS	122	7.382	7.003	27.747	1.00	12.10
ATOM	937	ND1	HIS	122	8.348	8.266	29.248	1.00	11.14
ATOM	938	CE1	HIS	122	8.905	7.070	29.328	1.00	11.31
ATOM	939	NE2	HIS	122	8.335	6.284	28.431	1.00	10.75
ATOM	940	C	HIS	122	4.455	10.255	26.753	1.00	12.85
ATOM	941	O	HIS	122	3.391	10.127	27.374	1.00	13.14
ATOM	942	N	GLY	123	4.724	11.291	25.973	1.00	13.41
ATOM	943	CA	GLY	123	3.767	12.371	25.838	1.00	14.75
ATOM	944	C	GLY	123	2.469	11.927	25.198	1.00	16.34
ATOM	945	O	GLY	123	1.398	12.472	25.519	1.00	17.30
ATOM	946	N	ILE	124	2.555	10.946	24.305	1.00	15.33
ATOM	947	CA	ILE	124	1.373	10.429	23.625	1.00	16.62
ATOM	948	CB	ILE	124	1.660	10.125	22.128	1.00	19.17
ATOM	949	CG2	ILE	124	2.685	9.029	21.991	1.00	20.31
ATOM	950	CG1	ILE	124	0.365	9.716	21.423	1.00	21.41
ATOM	951	CD1	ILE	124	-0.700	10.819	21.404	1.00	24.63
ATOM	952	C	ILE	124	0.840	9.193	24.325	1.00	15.39
ATOM	953	O	ILE	124	-0.067	8.535	23.821	1.00	16.38
ATOM	954	N	GLY	125	1.418	8.873	25.481	1.00	14.25
ATOM	955	CA	GLY	125	0.958	7.740	26.270	1.00	14.26
ATOM	956	C	GLY	125	1.420	6.364	25.839	1.00	14.37
ATOM	957	O	GLY	125	0.787	5.364	26.176	1.00	13.70
ATOM	958	N	ILE	126	2.512	6.304	25.087	1.00	14.23
ATOM	959	CA	ILE	126	3.021	5.012	24.644	1.00	14.92
ATOM	960	CB	ILE	126	3.259	4.960	23.088	1.00	17.26
ATOM	961	CG2	ILE	126	2.042	5.480	22.346	1.00	18.55
ATOM	962	CG1	ILE	126	4.559	5.667	22.723	1.00	21.12
ATOM	963	CD1	ILE	126	5.816	4.689	22.744	1.00	23.73
ATOM	964	C	ILE	126	4.355	4.674	25.332	1.00	13.61
ATOM	965	O	ILE	126	5.209	5.554	25.532	1.00	12.38

FIG.11B-23

ATOM	966	N	THR	127	4.514	3.416	25.725	1.00	12.02
ATOM	967	CA	THR	127	5.787	2.991	26.304	1.00	12.59
ATOM	968	CB	THR	127	5.630	2.446	27.729	1.00	13.49
ATOM	969	OG1	THR	127	5.288	3.516	28.613	1.00	21.14
ATOM	970	CG2	THR	127	6.923	1.830	28.190	1.00	8.53
ATOM	971	C	THR	127	6.362	1.951	25.381	1.00	11.65
ATOM	972	O	THR	127	5.646	1.065	24.907	1.00	12.97
ATOM	973	N	HIS	128	7.665	2.054	25.103	1.00	12.24
ATOM	974	CA	HIS	128	8.321	1.123	24.187	1.00	12.15
ATOM	975	CB	HIS	128	9.648	1.736	23.711	1.00	11.49
ATOM	976	CG	HIS	128	10.375	0.904	22.699	1.00	11.68
ATOM	977	CD2	HIS	128	10.471	1.012	21.350	1.00	11.46
ATOM	978	ND1	HIS	128	11.119	-0.200	23.050	1.00	11.90
ATOM	979	CE1	HIS	128	11.641	-0.741	21.961	1.00	12.68
ATOM	980	NE2	HIS	128	11.262	-0.025	20.915	1.00	12.57
ATOM	981	C	HIS	128	8.517	-0.242	24.817	1.00	12.15
ATOM	982	O	HIS	128	8.260	-1.275	24.192	1.00	11.72
ATOM	983	N	ARG	129	8.968	-0.236	26.070	1.00	11.07
ATOM	984	CA	ARG	129	9.191	-1.462	26.849	1.00	11.47
ATOM	985	CB	ARG	129	7.931	-2.343	26.858	1.00	12.32
ATOM	986	CG	ARG	129	6.807	-1.547	27.487	1.00	12.84
ATOM	987	CD	ARG	129	5.709	-2.441	28.097	1.00	12.85
ATOM	988	NE	ARG	129	4.988	-3.179	27.067	1.00	12.16
ATOM	989	CZ	ARG	129	3.911	-3.911	27.316	1.00	13.84
ATOM	990	NH1	ARG	129	3.446	-3.991	28.565	1.00	13.82
ATOM	991	NH2	ARG	129	3.304	-4.553	26.317	1.00	14.27
ATOM	992	C	ARG	129	10.380	-2.359	26.501	1.00	12.13
ATOM	993	O	ARG	129	10.592	-3.375	27.159	1.00	11.76
ATOM	994	N	ASP	130	11.162	-1.999	25.488	1.00	10.41
ATOM	995	CA	ASP	130	12.332	-2.823	25.147	1.00	11.17
ATOM	996	CB	ASP	130	11.914	-3.937	24.157	1.00	11.51
ATOM	997	CG	ASP	130	12.950	-5.082	24.156	1.00	13.34
ATOM	998	OD1	ASP	130	12.988	-5.895	23.184	1.00	13.30
ATOM	999	OD2	ASP	130	13.732	-5.178	25.127	1.00	13.23
ATOM	1000	C	ASP	130	13.442	-1.969	24.584	1.00	10.24
ATOM	1001	O	ASP	130	14.048	-2.300	23.564	1.00	10.99
ATOM	1002	N	ILE	131	13.735	-0.848	25.245	1.00	9.92
ATOM	1003	CA	ILE	131	14.787	0.047	24.763	1.00	10.16
ATOM	1004	CB	ILE	131	14.705	1.408	25.463	1.00	10.21
ATOM	1005	CG2	ILE	131	15.892	2.312	25.040	1.00	10.96
ATOM	1006	CG1	ILE	131	13.350	2.041	25.136	1.00	10.91
ATOM	1007	CD1	ILE	131	13.075	3.389	25.902	1.00	12.36

FIG.11B-24

ATOM	1008	C	ILE	131	16.152	-0.580	25.017	1.00	10.07
ATOM	1009	O	ILE	131	16.449	-0.979	26.134	1.00	11.34
ATOM	1010	N	LYS	132	16.969	-0.643	23.970	1.00	10.08
ATOM	1011	CA	LYS	132	18.314	-1.214	24.029	1.00	10.81
ATOM	1012	CB	LYS	132	18.256	-2.741	24.204	1.00	10.84
ATOM	1013	CG	LYS	132	17.367	-3.496	23.156	1.00	11.39
ATOM	1014	CD	LYS	132	17.443	-5.018	23.486	1.00	13.71
ATOM	1015	CE	LYS	132	16.477	-5.789	22.554	1.00	13.34
ATOM	1016	NZ	LYS	132	16.456	-7.271	22.822	1.00	13.78
ATOM	1017	C	LYS	132	18.974	-0.793	22.721	1.00	11.06
ATOM	1018	O	LYS	132	18.285	-0.412	21.767	1.00	12.07
ATOM	1019	N	PRO	133	20.307	-0.857	22.651	1.00	12.09
ATOM	1020	CD	PRO	133	21.235	-1.277	23.717	1.00	11.84
ATOM	1021	CA	PRO	133	21.040	-0.455	21.442	1.00	12.30
ATOM	1022	CB	PRO	133	22.499	-0.707	21.838	1.00	11.29
ATOM	1023	CG	PRO	133	22.486	-0.504	23.347	1.00	11.82
ATOM	1024	C	PRO	133	20.595	-1.090	20.156	1.00	13.29
ATOM	1025	O	PRO	133	20.667	-0.452	19.089	1.00	12.31
ATOM	1026	N	GLU	134	20.120	-2.335	20.236	1.00	13.34
ATOM	1027	CA	GLU	134	19.657	-3.033	19.047	1.00	14.29
ATOM	1028	CB	GLU	134	19.393	-4.512	19.354	1.00	15.51
ATOM	1029	CG	GLU	134	20.601	-5.281	19.934	1.00	16.70
ATOM	1030	CD	GLU	134	20.784	-5.274	21.434	1.00	18.54
ATOM	1031	OE1	GLU	134	20.556	-4.248	22.115	1.00	16.56
ATOM	1032	OE2	GLU	134	21.194	-6.364	21.905	1.00	19.18
ATOM	1033	C	GLU	134	18.372	-2.412	18.486	1.00	14.42
ATOM	1034	O	GLU	134	18.064	-2.566	17.293	1.00	14.80
ATOM	1035	N	ASN	135	17.625	-1.715	19.345	1.00	13.51
ATOM	1036	CA	ASN	135	16.367	-1.086	18.941	1.00	12.98
ATOM	1037	CB	ASN	135	15.252	-1.396	19.955	1.00	12.53
ATOM	1038	CG	ASN	135	14.698	-2.831	19.831	1.00	13.89
ATOM	1039	OD1	ASN	135	14.234	-3.421	20.815	1.00	15.19
ATOM	1040	ND2	ASN	135	14.730	-3.374	18.620	1.00	13.17
ATOM	1041	C	ASN	135	16.471	0.417	18.760	1.00	12.77
ATOM	1042	O	ASN	135	15.462	1.118	18.757	1.00	13.83
ATOM	1043	N	LEU	136	17.699	0.910	18.607	1.00	11.66
ATOM	1044	CA	LEU	136	17.953	2.330	18.386	1.00	12.25
ATOM	1045	CB	LEU	136	18.689	2.925	19.593	1.00	12.78
ATOM	1046	CG	LEU	136	17.899	2.887	20.912	1.00	12.80
ATOM	1047	CD1	LEU	136	18.839	3.437	22.009	1.00	13.44
ATOM	1048	CD2	LEU	136	16.599	3.711	20.833	1.00	14.59
ATOM	1049	C	LEU	136	18.779	2.378	17.091	1.00	13.15

FIG.11B-25

ATOM	1050	O	LEU	136	19.957	2.043	17.084	1.00	13.18
ATOM	1051	N	LEU	137	18.124	2.735	15.991	1.00	13.60
ATOM	1052	CA	LEU	137	18.783	2.775	14.692	1.00	14.28
ATOM	1053	CB	LEU	137	17.814	2.291	13.611	1.00	14.14
ATOM	1054	CG	LEU	137	17.210	0.941	14.025	1.00	15.38
ATOM	1055	CD1	LEU	137	16.280	0.448	12.879	1.00	14.24
ATOM	1056	CD2	LEU	137	18.300	-0.074	14.319	1.00	15.67
ATOM	1057	C	LEU	137	19.287	4.124	14.359	1.00	15.19
ATOM	1058	O	LEU	137	18.884	5.118	14.952	1.00	15.24
ATOM	1059	N	LEU	138	20.174	4.178	13.372	1.00	16.26
ATOM	1060	CA	LEU	138	20.779	5.433	12.952	1.00	16.85
ATOM	1061	CB	LEU	138	22.296	5.385	13.183	1.00	17.95
ATOM	1062	CG	LEU	138	22.811	5.144	14.617	1.00	19.40
ATOM	1063	CD1	LEU	138	22.251	6.225	15.531	1.00	19.08
ATOM	1064	CD2	LEU	138	22.399	3.760	15.102	1.00	22.69
ATOM	1065	C	LEU	138	20.534	5.671	11.461	1.00	17.74
ATOM	1066	O	LEU	138	20.604	4.731	10.676	1.00	17.49
ATOM	1067	N	ASP	139	20.236	6.913	11.083	1.00	18.21
ATOM	1068	CA	ASP	139	20.013	7.235	9.673	1.00	20.36
ATOM	1069	CB	ASP	139	18.989	8.371	9.527	1.00	20.49
ATOM	1070	CG	ASP	139	19.372	9.764	9.970	1.00	20.35
ATOM	1071	OD1	ASP	139	18.491	10.652	9.888	1.00	23.24
ATOM	1072	OD2	ASP	139	20.517	10.002	10.389	1.00	21.14
ATOM	1073	C	ASP	139	21.345	7.624	9.073	1.00	21.49
ATOM	1074	O	ASP	139	22.381	7.469	9.709	1.00	20.83
ATOM	1075	N	GLU	140	21.330	8.115	7.836	1.00	23.55
ATOM	1076	CA	GLU	140	22.564	8.511	7.169	1.00	25.49
ATOM	1077	CB	GLU	140	22.282	8.952	5.726	1.00	27.10
ATOM	1078	CG	GLU	140	21.287	10.082	5.469	1.00	30.90
ATOM	1079	CD	GLU	140	19.954	9.585	5.973	1.00	32.27
ATOM	1080	OE1	GLU	140	19.575	8.466	5.572	1.00	34.20
ATOM	1081	OE2	GLU	140	19.282	10.287	6.757	1.00	35.13
ATOM	1082	C	GLU	140	23.386	9.625	7.867	1.00	25.97
ATOM	1083	O	GLU	140	24.593	9.727	7.649	1.00	26.62
ATOM	1084	N	ARG	141	22.736	10.444	8.692	1.00	26.36
ATOM	1085	CA	ARG	141	23.432	11.515	9.408	1.00	26.34
ATOM	1086	CB	ARG	141	22.628	12.821	9.362	1.00	28.11
ATOM	1087	CG	ARG	141	22.492	13.508	7.970	1.00	30.79
ATOM	1088	CD	ARG	141	21.702	14.853	7.950	1.00	32.84
ATOM	1089	NE	ARG	141	22.291	15.861	8.833	1.00	35.77
ATOM	1090	CZ	ARG	141	21.964	16.036	10.113	1.00	37.04
ATOM	1091	NH1	ARG	141	21.039	15.271	10.681	1.00	36.95

FIG.11B-26

ATOM	1092	NH2	ARG	141	22.564	16.981	10.828	1.00	37.88
ATOM	1093	C	ARG	141	23.645	11.156	10.879	1.00	25.65
ATOM	1094	O	ARG	141	23.877	12.026	11.720	1.00	25.46
ATOM	1095	N	ASP	142	23.579	9.868	11.184	1.00	23.88
ATOM	1096	CA	ASP	142	23.755	9.403	12.559	1.00	23.96
ATOM	1097	CB	ASP	142	25.128	9.800	13.107	1.00	26.22
ATOM	1098	CG	ASP	142	26.194	8.903	12.523	1.00	28.88
ATOM	1099	OD1	ASP	142	25.919	7.694	12.418	1.00	29.81
ATOM	1100	OD2	ASP	142	27.300	9.375	12.182	1.00	31.98
ATOM	1101	C	ASP	142	22.677	9.917	13.533	1.00	22.68
ATOM	1102	O	ASP	142	22.940	10.092	14.729	1.00	21.46
ATOM	1103	N	ASN	143	21.475	10.172	13.025	1.00	21.05
ATOM	1104	CA	ASN	143	20.387	10.603	13.909	1.00	19.86
ATOM	1105	CB	ASN	143	19.326	11.401	13.156	1.00	19.72
ATOM	1106	CG	ASN	143	19.848	12.766	12.784	1.00	20.89
ATOM	1107	OD1	ASN	143	19.752	13.190	11.621	1.00	23.00
ATOM	1108	ND2	ASN	143	20.404	13.472	13.762	1.00	18.41
ATOM	1109	C	ASN	143	19.749	9.348	14.453	1.00	18.33
ATOM	1110	O	ASN	143	19.447	8.437	13.698	1.00	18.35
ATOM	1111	N	LEU	144	19.536	9.295	15.766	1.00	16.77
ATOM	1112	CA	LEU	144	18.957	8.108	16.383	1.00	16.09
ATOM	1113	CB	LEU	144	19.337	8.075	17.867	1.00	15.65
ATOM	1114	CG	LEU	144	18.727	7.080	18.855	1.00	14.93
ATOM	1115	CD1	LEU	144	19.744	6.887	19.992	1.00	14.95
ATOM	1116	CD2	LEU	144	17.374	7.585	19.387	1.00	15.73
ATOM	1117	C	LEU	144	17.450	8.022	16.194	1.00	15.54
ATOM	1118	O	LEU	144	16.739	9.029	16.265	1.00	15.24
ATOM	1119	N	LYS	145	16.973	6.800	15.972	1.00	14.42
ATOM	1120	CA	LYS	145	15.557	6.557	15.744	1.00	15.14
ATOM	1121	CB	LYS	145	15.295	6.210	14.277	1.00	15.62
ATOM	1122	CG	LYS	145	15.953	7.083	13.201	1.00	18.61
ATOM	1123	CD	LYS	145	15.096	8.291	13.029	1.00	19.20
ATOM	1124	CE	LYS	145	15.797	9.269	12.033	1.00	19.98
ATOM	1125	NZ	LYS	145	14.861	10.344	11.574	1.00	19.93
ATOM	1126	C	LYS	145	15.126	5.339	16.535	1.00	13.97
ATOM	1127	O	LYS	145	15.655	4.248	16.329	1.00	13.07
ATOM	1128	N	ILE	146	14.166	5.526	17.436	1.00	13.48
ATOM	1129	CA	ILE	146	13.654	4.417	18.238	1.00	12.91
ATOM	1130	CB	ILE	146	12.723	4.928	19.336	1.00	12.90
ATOM	1131	CG2	ILE	146	12.066	3.737	20.070	1.00	13.04
ATOM	1132	CG1	ILE	146	13.538	5.762	20.324	1.00	13.51
ATOM	1133	CD1	ILE	146	12.694	6.479	21.403	1.00	13.33

FIG.11B-27

ATOM	1134	C	ILE	146	12.901	3.476	17.301	1.00	13.05
ATOM	1135	O	ILE	146	12.012	3.904	16.559	1.00	12.88
ATOM	1136	N	SER	147	13.238	2.192	17.382	1.00	12.43
ATOM	1137	CA	SER	147	12.681	1.173	16.496	1.00	13.35
ATOM	1138	CB	SER	147	13.822	0.665	15.593	1.00	14.71
ATOM	1139	OG	SER	147	13.489	-0.508	14.855	1.00	15.66
ATOM	1140	C	SER	147	12.038	-0.011	17.174	1.00	14.00
ATOM	1141	O	SER	147	12.369	-0.344	18.318	1.00	12.67
ATOM	1142	N	ASP	148	11.110	-0.640	16.451	1.00	14.20
ATOM	1143	CA	ASP	148	10.417	-1.855	16.883	1.00	14.80
ATOM	1144	CB	ASP	148	11.453	-2.915	17.282	1.00	16.84
ATOM	1145	CG	ASP	148	10.867	-4.294	17.493	1.00	19.50
ATOM	1146	OD1	ASP	148	11.660	-5.228	17.723	1.00	23.01
ATOM	1147	OD2	ASP	148	9.636	-4.457	17.430	1.00	19.78
ATOM	1148	C	ASP	148	9.426	-1.695	17.980	1.00	15.21
ATOM	1149	O	ASP	148	9.767	-1.794	19.152	1.00	15.83
ATOM	1150	N	PHE	149	8.166	-1.494	17.610	1.00	14.13
ATOM	1151	CA	PHE	149	7.101	-1.309	18.585	1.00	14.87
ATOM	1152	CB	PHE	149	6.252	-0.114	18.143	1.00	15.09
ATOM	1153	CG	PHE	149	6.974	1.187	18.274	1.00	15.25
ATOM	1154	CD1	PHE	149	7.860	1.608	17.292	1.00	15.38
ATOM	1155	CD2	PHE	149	6.844	1.952	19.440	1.00	14.86
ATOM	1156	CE1	PHE	149	8.623	2.776	17.464	1.00	14.94
ATOM	1157	CE2	PHE	149	7.599	3.114	19.621	1.00	14.99
ATOM	1158	CZ	PHE	149	8.487	3.524	18.636	1.00	14.89
ATOM	1159	C	PHE	149	6.304	-2.544	18.811	1.00	15.24
ATOM	1160	O	PHE	149	5.145	-2.484	19.220	1.00	16.36
ATOM	1161	N	GLY	150	6.936	-3.691	18.572	1.00	16.17
ATOM	1162	CA	GLY	150	6.269	-4.970	18.746	1.00	16.47
ATOM	1163	C	GLY	150	5.947	-5.286	20.197	1.00	16.83
ATOM	1164	O	GLY	150	5.093	-6.126	20.481	1.00	17.90
ATOM	1165	N	LEU	151	6.621	-4.626	21.127	1.00	15.78
ATOM	1166	CA	LEU	151	6.326	-4.871	22.541	1.00	16.37
ATOM	1167	CB	LEU	151	7.584	-5.298	23.292	1.00	17.64
ATOM	1168	CG	LEU	151	8.078	-6.619	22.700	1.00	19.89
ATOM	1169	CD1	LEU	151	9.341	-6.989	23.457	1.00	19.60
ATOM	1170	CD2	LEU	151	7.040	-7.730	22.782	1.00	20.88
ATOM	1171	C	LEU	151	5.729	-3.663	23.222	1.00	15.93
ATOM	1172	O	LEU	151	5.392	-3.723	24.405	1.00	16.32
ATOM	1173	N	ALA	152	5.567	-2.577	22.466	1.00	14.33
ATOM	1174	CA	ALA	152	5.020	-1.329	22.994	1.00	14.78
ATOM	1175	CB	ALA	152	5.196	-0.205	21.964	1.00	14.02

FIG.11B-28

ATOM	1176	C	ALA	152	3.559	-1.412	23.400	1.00	14.74
ATOM	1177	O	ALA	152	2.820	-2.287	22.946	1.00	16.44
ATOM	1178	N	THR	153	3.134	-0.498	24.262	1.00	14.29
ATOM	1179	CA	THR	153	1.736	-0.486	24.678	1.00	14.48
ATOM	1180	CB	THR	153	1.465	-1.570	25.767	1.00	15.01
ATOM	1181	OG1	THR	153	0.052	-1.803	25.857	1.00	15.18
ATOM	1182	CG2	THR	153	1.985	-1.140	27.135	1.00	16.34
ATOM	1183	C	THR	153	1.305	0.866	25.134	1.00	14.74
ATOM	1184	O	THR	153	2.124	1.764	25.321	1.00	14.16
ATOM	1185	N	VAL	154	-0.002	1.036	25.283	1.00	15.49
ATOM	1186	CA	VAL	154	-0.574	2.294	25.744	1.00	16.27
ATOM	1187	CB	VAL	154	-2.024	2.446	25.187	1.00	17.58
ATOM	1188	CG1	VAL	154	-2.721	3.669	25.796	1.00	18.88
ATOM	1189	CG2	VAL	154	-1.978	2.573	23.672	1.00	18.48
ATOM	1190	C	VAL	154	-0.584	2.280	27.288	1.00	16.33
ATOM	1191	O	VAL	154	-1.096	1.337	27.896	1.00	17.03
ATOM	1192	N	PHE	155	0.002	3.296	27.917	1.00	14.86
ATOM	1193	CA	PHE	155	-0.011	3.348	29.372	1.00	14.65
ATOM	1194	CB	PHE	155	1.411	3.401	29.968	1.00	13.64
ATOM	1195	CG	PHE	155	2.088	4.733	29.830	1.00	12.64
ATOM	1196	CD1	PHE	155	2.810	5.044	28.675	1.00	11.40
ATOM	1197	CD2	PHE	155	1.984	5.696	30.836	1.00	12.17
ATOM	1198	CE1	PHE	155	3.412	6.282	28.520	1.00	12.13
ATOM	1199	CE2	PHE	155	2.592	6.960	30.691	1.00	13.02
ATOM	1200	CZ	PHE	155	3.311	7.254	29.522	1.00	12.14
ATOM	1201	C	PHE	155	-0.830	4.566	29.831	1.00	14.29
ATOM	1202	O	PHE	155	-1.041	4.748	31.027	1.00	14.95
ATOM	1203	N	ARG	156	-1.257	5.406	28.888	1.00	14.44
ATOM	1204	CA	ARG	156	-2.082	6.570	29.246	1.00	14.70
ATOM	1205	CB	ARG	156	-1.241	7.846	29.410	1.00	15.59
ATOM	1206	CG	ARG	156	-2.174	8.962	30.089	1.00	17.04
ATOM	1207	CD	ARG	156	-1.525	10.389	29.970	1.00	18.38
ATOM	1208	NE	ARG	156	-0.159	10.425	30.482	1.00	18.17
ATOM	1209	CZ	ARG	156	0.922	10.609	29.719	1.00	18.70
ATOM	1210	NH1	ARG	156	0.795	10.779	28.411	1.00	18.30
ATOM	1211	NH2	ARG	156	2.131	10.605	30.265	1.00	19.27
ATOM	1212	C	ARG	156	-3.100	6.807	28.154	1.00	14.58
ATOM	1213	O	ARG	156	-2.753	6.945	26.984	1.00	14.45
ATOM	1214	N	TYR	157	-4.372	6.858	28.541	1.00	14.25
ATOM	1215	CA	TYR	157	-5.441	7.060	27.574	1.00	14.50
ATOM	1216	CB	TYR	157	-6.040	5.715	27.173	1.00	15.15
ATOM	1217	CG	TYR	157	-6.845	5.770	25.902	1.00	15.19

FIG.11B-29

ATOM	1218	CD1	TYR	157	-6.219	5.814	24.653	1.00	16.14
ATOM	1219	CE1	TYR	157	-6.965	5.864	23.472	1.00	16.78
ATOM	1220	CD2	TYR	157	-8.232	5.780	25.945	1.00	15.85
ATOM	1221	CE2	TYR	157	-8.987	5.832	24.783	1.00	17.07
ATOM	1222	CZ	TYR	157	-8.356	5.875	23.548	1.00	17.48
ATOM	1223	OH	TYR	157	-9.129	5.956	22.403	1.00	17.82
ATOM	1224	C	TYR	157	-6.507	7.890	28.231	1.00	15.01
ATOM	1225	O	TYR	157	-6.867	7.632	29.379	1.00	15.42
ATOM	1226	N	ASN	158	-7.013	8.887	27.505	1.00	16.30
ATOM	1227	CA	ASN	158	-8.033	9.786	28.047	1.00	16.67
ATOM	1228	CB	ASN	158	-9.345	9.023	28.285	1.00	16.49
ATOM	1229	CG	ASN	158	-10.097	8.800	26.961	1.00	15.70
ATOM	1230	OD1	ASN	158	-10.988	7.954	26.882	1.00	16.14
ATOM	1231	ND2	ASN	158	-9.741	9.569	25.927	1.00	13.85
ATOM	1232	C	ASN	158	-7.543	10.420	29.336	1.00	18.61
ATOM	1233	O	ASN	158	-8.312	10.640	30.278	1.00	17.84
ATOM	1234	N	ASN	159	-6.242	10.706	29.348	1.00	19.74
ATOM	1235	CA	ASN	159	-5.530	11.321	30.462	1.00	22.33
ATOM	1236	CB	ASN	159	-6.099	12.713	30.758	1.00	24.30
ATOM	1237	CG	ASN	159	-4.976	13.515	31.438	1.00	26.68
ATOM	1238	OD1	ASN	159	-3.879	13.667	30.885	1.00	28.50
ATOM	1239	ND2	ASN	159	-5.249	14.021	32.633	1.00	29.10
ATOM	1240	C	ASN	159	-5.522	10.478	31.742	1.00	22.20
ATOM	1241	O	ASN	159	-5.259	10.992	32.824	1.00	24.01
ATOM	1242	N	ARG	160	-5.808	9.185	31.621	1.00	21.47
ATOM	1243	CA	ARG	160	-5.803	8.298	32.781	1.00	20.69
ATOM	1244	CB	ARG	160	-7.141	7.559	32.907	1.00	23.48
ATOM	1245	CG	ARG	160	-8.091	8.097	34.011	1.00	28.38
ATOM	1246	CD	ARG	160	-7.621	7.848	35.471	1.00	30.43
ATOM	1247	NE	ARG	160	-8.739	7.883	36.411	1.00	34.64
ATOM	1248	CZ	ARG	160	-9.202	8.978	37.008	1.00	35.54
ATOM	1249	NH1	ARG	160	-8.640	10.160	36.779	1.00	36.58
ATOM	1250	NH2	ARG	160	-10.246	8.890	37.829	1.00	37.21
ATOM	1251	C	ARG	160	-4.668	7.290	32.612	1.00	19.16
ATOM	1252	O	ARG	160	-4.591	6.601	31.602	1.00	18.07
ATOM	1253	N	GLU	161	-3.778	7.225	33.597	1.00	17.48
ATOM	1254	CA	GLU	161	-2.654	6.297	33.530	1.00	17.30
ATOM	1255	CB	GLU	161	-1.528	6.741	34.468	1.00	16.64
ATOM	1256	CG	GLU	161	-0.264	5.834	34.412	1.00	16.91
ATOM	1257	CD	GLU	161	0.821	6.223	35.416	1.00	18.42
ATOM	1258	OE1	GLU	161	1.882	5.569	35.377	1.00	16.94
ATOM	1259	OE2	GLU	161	0.606	7.154	36.224	1.00	19.58

FIG.11B-30

ATOM	1260	C	GLU	161	-3.060	4.909	33.903	1.00	17.47
ATOM	1261	O	GLU	161	-3.846	4.696	34.836	1.00	17.69
ATOM	1262	N	ARG	162	-2.522	3.941	33.177	1.00	18.18
ATOM	1263	CA	ARG	162	-2.785	2.536	33.425	1.00	18.75
ATOM	1264	CB	ARG	162	-3.133	1.824	32.121	1.00	22.41
ATOM	1265	CG	ARG	162	-3.510	0.361	32.099	1.00	26.57
ATOM	1266	CD	ARG	162	-4.025	0.042	30.639	1.00	29.14
ATOM	1267	NE	ARG	162	-5.085	0.956	30.197	1.00	32.40
ATOM	1268	CZ	ARG	162	-5.832	0.771	29.106	1.00	32.85
ATOM	1269	NH1	ARG	162	-6.771	1.651	28.776	1.00	33.54
ATOM	1270	NH2	ARG	162	-5.649	-0.301	28.346	1.00	33.73
ATOM	1271	C	ARG	162	-1.485	1.899	33.950	1.00	17.95
ATOM	1272	O	ARG	162	-0.453	2.015	33.296	1.00	17.82
ATOM	1273	N	LEU	163	-1.532	1.248	35.113	1.00	16.28
ATOM	1274	CA	LEU	163	-0.330	0.593	35.641	1.00	15.46
ATOM	1275	CB	LEU	163	-0.493	0.202	37.117	1.00	16.31
ATOM	1276	CG	LEU	163	-0.758	1.459	37.945	1.00	16.62
ATOM	1277	CD1	LEU	163	-1.147	1.014	39.334	1.00	17.07
ATOM	1278	CD2	LEU	163	0.467	2.387	37.975	1.00	16.61
ATOM	1279	C	LEU	163	-0.113	-0.686	34.842	1.00	15.82
ATOM	1280	O	LEU	163	-1.077	-1.349	34.424	1.00	16.39
ATOM	1281	N	LEU	164	1.147	-1.031	34.611	1.00	14.65
ATOM	1282	CA	LEU	164	1.465	-2.231	33.842	1.00	15.17
ATOM	1283	CB	LEU	164	2.642	-1.950	32.903	1.00	15.48
ATOM	1284	CG	LEU	164	2.340	-0.814	31.914	1.00	16.69
ATOM	1285	CD1	LEU	164	3.528	-0.691	30.973	1.00	17.58
ATOM	1286	CD2	LEU	164	1.084	-1.060	31.127	1.00	18.21
ATOM	1287	C	LEU	164	1.811	-3.403	34.730	1.00	14.77
ATOM	1288	O	LEU	164	2.200	-3.219	35.883	1.00	15.24
ATOM	1289	N	ASN	165	1.678	-4.616	34.197	1.00	15.82
ATOM	1290	CA	ASN	165	2.017	-5.809	34.962	1.00	17.49
ATOM	1291	CB	ASN	165	0.760	-6.388	35.633	1.00	18.54
ATOM	1292	CG	ASN	165	-0.289	-6.794	34.623	1.00	18.94
ATOM	1293	OD1	ASN	165	-1.310	-6.122	34.458	1.00	21.86
ATOM	1294	ND2	ASN	165	-0.038	-7.887	33.929	1.00	18.29
ATOM	1295	C	ASN	165	2.692	-6.894	34.084	1.00	18.31
ATOM	1296	O	ASN	165	3.203	-7.887	34.595	1.00	19.20
ATOM	1297	N	LYS	166	2.701	-6.687	32.773	1.00	18.68
ATOM	1298	CA	LYS	166	3.297	-7.664	31.862	1.00	20.26
ATOM	1299	CB	LYS	166	2.916	-7.359	30.408	1.00	21.66
ATOM	1300	CG	LYS	166	3.530	-8.249	29.267	1.00	24.00
ATOM	1301	CD	LYS	166	3.333	-7.673	27.802	1.00	26.84

FIG.11B-31

ATOM	1302	CE	LYS	166	3.949	-8.340	26.520	1.00	27.03
ATOM	1303	NZ	LYS	166	5.449	-8.227	26.415	1.00	28.54
ATOM	1304	C	LYS	166	4.794	-7.686	31.950	1.00	20.70
ATOM	1305	O	LYS	166	5.447	-6.639	31.963	1.00	18.98
ATOM	1306	N	MET	167	5.355	-8.886	32.019	1.00	21.49
ATOM	1307	CA	MET	167	6.800	-9.013	32.071	1.00	23.10
ATOM	1308	CB	MET	167	7.203	-10.281	32.863	1.00	26.20
ATOM	1309	CG	MET	167	7.427	-10.090	34.463	1.00	29.77
ATOM	1310	SD	MET	167	7.743	-11.672	35.352	1.00	36.62
ATOM	1311	CE	MET	167	6.109	-12.412	35.356	1.00	34.01
ATOM	1312	C	MET	167	7.298	-9.031	30.615	1.00	22.75
ATOM	1313	O	MET	167	6.861	-9.837	29.789	1.00	22.16
ATOM	1314	N	CYS	168	8.169	-8.083	30.292	1.00	21.44
ATOM	1315	CA	CYS	168	8.750	-8.011	28.963	1.00	20.77
ATOM	1316	CB	CYS	168	7.754	-7.523	27.926	1.00	22.35
ATOM	1317	SG	CYS	168	6.960	-5.964	28.305	1.00	26.07
ATOM	1318	C	CYS	168	9.915	-7.126	28.970	1.00	18.90
ATOM	1319	O	CYS	168	10.132	-6.357	29.914	1.00	17.73
ATOM	1320	N	GLY	169	10.696	-7.219	27.903	1.00	17.73
ATOM	1321	CA	GLY	169	11.908	-6.437	27.812	1.00	15.14
ATOM	1322	C	GLY	169	13.074	-7.384	27.579	1.00	15.05
ATOM	1323	O	GLY	169	12.889	-8.485	27.043	1.00	14.39
ATOM	1324	N	THR	170	14.264	-6.957	27.990	1.00	12.82
ATOM	1325	CA	THR	170	15.498	-7.726	27.817	1.00	13.82
ATOM	1326	CB	THR	170	16.278	-7.119	26.624	1.00	12.90
ATOM	1327	OG1	THR	170	15.476	-7.208	25.432	1.00	13.36
ATOM	1328	CG2	THR	170	17.582	-7.853	26.399	1.00	14.59
ATOM	1329	C	THR	170	16.183	-7.607	29.174	1.00	13.27
ATOM	1330	O	THR	170	16.504	-6.502	29.615	1.00	13.03
ATOM	1331	N	LEU	171	16.412	-8.744	29.830	1.00	13.36
ATOM	1332	CA	LEU	171	16.961	-8.761	31.187	1.00	14.06
ATOM	1333	CB	LEU	171	17.427	-10.190	31.522	1.00	15.16
ATOM	1334	CG	LEU	171	16.873	-10.997	32.714	1.00	20.32
ATOM	1335	CD1	LEU	171	15.558	-10.455	33.272	1.00	17.54
ATOM	1336	CD2	LEU	171	16.747	-12.464	32.274	1.00	18.34
ATOM	1337	C	LEU	171	18.032	-7.726	31.600	1.00	13.09
ATOM	1338	O	LEU	171	17.877	-7.043	32.629	1.00	12.73
ATOM	1339	N	PRO	172	19.128	-7.608	30.836	1.00	12.83
ATOM	1340	CD	PRO	172	19.556	-8.419	29.679	1.00	13.47
ATOM	1341	CA	PRO	172	20.161	-6.633	31.212	1.00	12.48
ATOM	1342	CB	PRO	172	21.238	-6.839	30.147	1.00	12.98
ATOM	1343	CG	PRO	172	21.049	-8.280	29.732	1.00	13.76

FIG.11B-32

ATOM	1344	C	PRO	172	19.673	-5.187	31.274	1.00	12.70
ATOM	1345	O	PRO	172	20.249	-4.360	31.993	1.00	12.82
ATOM	1346	N	TYR	173	18.624	-4.894	30.521	1.00	11.48
ATOM	1347	CA	TYR	173	18.062	-3.547	30.452	1.00	11.83
ATOM	1348	CB	TYR	173	17.718	-3.207	29.009	1.00	12.45
ATOM	1349	CG	TYR	173	18.897	-3.324	28.087	1.00	12.78
ATOM	1350	CD1	TYR	173	19.693	-2.222	27.820	1.00	13.91
ATOM	1351	CE1	TYR	173	20.812	-2.319	26.989	1.00	14.46
ATOM	1352	CD2	TYR	173	19.236	-4.546	27.501	1.00	13.62
ATOM	1353	CE2	TYR	173	20.347	-4.657	26.668	1.00	15.04
ATOM	1354	CZ	TYR	173	21.128	-3.539	26.419	1.00	15.41
ATOM	1355	OH	TYR	173	22.231	-3.623	25.594	1.00	18.27
ATOM	1356	C	TYR	173	16.771	-3.330	31.236	1.00	12.34
ATOM	1357	O	TYR	173	16.294	-2.199	31.346	1.00	11.61
ATOM	1358	N	VAL	174	16.205	-4.388	31.800	1.00	12.77
ATOM	1359	CA	VAL	174	14.927	-4.226	32.484	1.00	12.44
ATOM	1360	CB	VAL	174	14.149	-5.562	32.469	1.00	14.29
ATOM	1361	CG1	VAL	174	14.648	-6.479	33.574	1.00	15.43
ATOM	1362	CG2	VAL	174	12.646	-5.292	32.580	1.00	14.81
ATOM	1363	C	VAL	174	15.052	-3.659	33.929	1.00	12.17
ATOM	1364	O	VAL	174	16.020	-3.917	34.619	1.00	12.63
ATOM	1365	N	ALA	175	14.059	-2.869	34.324	1.00	11.21
ATOM	1366	CA	ALA	175	14.018	-2.252	35.654	1.00	11.66
ATOM	1367	CB	ALA	175	12.929	-1.210	35.686	1.00	13.92
ATOM	1368	C	ALA	175	13.755	-3.319	36.743	1.00	11.10
ATOM	1369	O	ALA	175	12.995	-4.250	36.529	1.00	12.27
ATOM	1370	N	PRO	176	14.346	-3.148	37.928	1.00	11.44
ATOM	1371	CD	PRO	176	15.232	-2.035	38.314	1.00	12.40
ATOM	1372	CA	PRO	176	14.174	-4.106	39.026	1.00	12.63
ATOM	1373	CB	PRO	176	15.124	-3.569	40.097	1.00	12.54
ATOM	1374	CG	PRO	176	15.164	-2.081	39.831	1.00	12.85
ATOM	1375	C	PRO	176	12.734	-4.318	39.479	1.00	13.15
ATOM	1376	O	PRO	176	12.368	-5.422	39.919	1.00	13.29
ATOM	1377	N	GLU	177	11.906	-3.292	39.346	1.00	12.90
ATOM	1378	CA	GLU	177	10.525	-3.432	39.788	1.00	14.16
ATOM	1379	CB	GLU	177	9.798	-2.087	39.740	1.00	14.13
ATOM	1380	CG	GLU	177	9.624	-1.333	38.419	1.00	13.02
ATOM	1381	CD	GLU	177	10.815	-0.414	38.186	1.00	13.91
ATOM	1382	OE1	GLU	177	10.624	0.519	37.371	1.00	13.00
ATOM	1383	OE2	GLU	177	11.914	-0.606	38.767	1.00	13.08
ATOM	1384	C	GLU	177	9.746	-4.486	38.978	1.00	15.90
ATOM	1385	O	GLU	177	8.798	-5.064	39.482	1.00	17.12

FIG.11B-33

ATOM	1386	N	LEU	178	10.129	-4.729	37.726	1.00	16.49
ATOM	1387	CA	LEU	178	9.424	-5.742	36.943	1.00	19.28
ATOM	1388	CB	LEU	178	9.957	-5.804	35.506	1.00	22.15
ATOM	1389	CG	LEU	178	9.454	-6.848	34.501	1.00	24.53
ATOM	1390	CD1	LEU	178	10.036	-8.220	34.827	1.00	25.14
ATOM	1391	CD2	LEU	178	7.927	-6.873	34.518	1.00	25.07
ATOM	1392	C	LEU	178	9.622	-7.096	37.565	1.00	20.37
ATOM	1393	O	LEU	178	8.739	-7.954	37.516	1.00	20.98
ATOM	1394	N	LEU	179	10.791	-7.302	38.155	1.00	20.27
ATOM	1395	CA	LEU	179	11.101	-8.584	38.766	1.00	21.63
ATOM	1396	CB	LEU	179	12.617	-8.838	38.700	1.00	21.75
ATOM	1397	CG	LEU	179	13.233	-8.817	37.294	1.00	23.23
ATOM	1398	CD1	LEU	179	14.748	-8.931	37.351	1.00	22.87
ATOM	1399	CD2	LEU	179	12.639	-9.954	36.485	1.00	22.80
ATOM	1400	C	LEU	179	10.628	-8.700	40.202	1.00	22.23
ATOM	1401	O	LEU	179	10.591	-9.799	40.767	1.00	24.11
ATOM	1402	N	LYS	180	10.230	-7.594	40.810	1.00	21.86
ATOM	1403	CA	LYS	180	9.827	-7.680	42.212	1.00	22.25
ATOM	1404	CB	LYS	180	10.813	-6.909	43.092	1.00	24.33
ATOM	1405	CG	LYS	180	10.945	-5.385	42.935	1.00	27.64
ATOM	1406	CD	LYS	180	11.950	-4.753	43.967	1.00	30.62
ATOM	1407	CE	LYS	180	13.334	-5.432	43.916	1.00	31.90
ATOM	1408	NZ	LYS	180	14.305	-4.830	44.871	1.00	34.05
ATOM	1409	C	LYS	180	8.454	-7.213	42.594	1.00	21.51
ATOM	1410	O	LYS	180	8.007	-7.463	43.718	1.00	21.61
ATOM	1411	N	ARG	181	7.760	-6.547	41.680	1.00	20.15
ATOM	1412	CA	ARG	181	6.438	-6.015	41.981	1.00	19.69
ATOM	1413	CB	ARG	181	6.455	-4.483	41.919	1.00	20.79
ATOM	1414	CG	ARG	181	7.705	-3.742	42.554	1.00	23.16
ATOM	1415	CD	ARG	181	8.028	-2.949	43.866	1.00	27.13
ATOM	1416	NE	ARG	181	7.696	-3.723	45.039	1.00	26.61
ATOM	1417	CZ	ARG	181	8.122	-3.493	46.281	1.00	27.46
ATOM	1418	NH1	ARG	181	7.708	-4.294	47.244	1.00	25.45
ATOM	1419	NH2	ARG	181	8.959	-2.501	46.570	1.00	29.25
ATOM	1420	C	ARG	181	5.384	-6.516	40.995	1.00	19.43
ATOM	1421	O	ARG	181	5.679	-6.774	39.818	1.00	18.33
ATOM	1422	N	ARG	182	4.153	-6.673	41.468	1.00	18.70
ATOM	1423	CA	ARG	182	3.090	-7.125	40.576	1.00	19.47
ATOM	1424	CB	ARG	182	1.813	-7.460	41.348	1.00	22.25
ATOM	1425	CG	ARG	182	0.886	-8.101	40.297	1.00	26.02
ATOM	1426	CD	ARG	182	-0.443	-8.656	40.836	1.00	27.77
ATOM	1427	NE	ARG	182	-1.305	-7.590	41.330	1.00	31.09

FIG.11B-34

ATOM	1428	CZ	ARG	182	-2.507	-7.787	41.859	1.00	33.26
ATOM	1429	NH1	ARG	182	-2.995	-9.017	41.970	1.00	34.85
ATOM	1430	NH2	ARG	182	-3.225	-6.749	42.269	1.00	34.56
ATOM	1431	C	ARG	182	2.728	-6.068	39.537	1.00	18.40
ATOM	1432	O	ARG	182	2.482	-6.397	38.372	1.00	19.29
ATOM	1433	N	GLU	183	2.668	-4.808	39.958	1.00	17.24
ATOM	1434	CA	GLU	183	2.337	-3.715	39.049	1.00	16.19
ATOM	1435	CB	GLU	183	0.974	-3.102	39.394	1.00	17.54
ATOM	1436	CG	GLU	183	-0.225	-4.044	39.253	1.00	19.75
ATOM	1437	CD	GLU	183	-1.439	-3.182	39.621	1.00	21.38
ATOM	1438	OE1	GLU	183	-1.593	-2.835	40.813	1.00	23.31
ATOM	1439	OE2	GLU	183	-2.208	-2.855	38.697	1.00	21.76
ATOM	1440	C	GLU	183	3.387	-2.621	39.147	1.00	15.05
ATOM	1441	O	GLU	183	4.085	-2.503	40.148	1.00	13.47
ATOM	1442	N	PHE	184	3.480	-1.797	38.111	1.00	14.19
ATOM	1443	CA	PHE	184	4.474	-0.738	38.107	1.00	14.24
ATOM	1444	CB	PHE	184	5.861	-1.343	37.825	1.00	14.97
ATOM	1445	CG	PHE	184	5.849	-2.409	36.762	1.00	13.01
ATOM	1446	CD1	PHE	184	5.814	-2.079	35.414	1.00	14.32
ATOM	1447	CD2	PHE	184	5.768	-3.752	37.122	1.00	13.96
ATOM	1448	CE1	PHE	184	5.688	-3.068	34.441	1.00	14.25
ATOM	1449	CE2	PHE	184	5.637	-4.754	36.154	1.00	13.88
ATOM	1450	CZ	PHE	184	5.595	-4.407	34.814	1.00	14.77
ATOM	1451	C	PHE	184	4.138	0.318	37.093	1.00	14.04
ATOM	1452	O	PHE	184	3.427	0.063	36.120	1.00	12.37
ATOM	1453	N	HIS	185	4.631	1.524	37.342	1.00	12.36
ATOM	1454	CA	HIS	185	4.442	2.649	36.434	1.00	13.40
ATOM	1455	CB	HIS	185	4.892	3.934	37.121	1.00	13.03
ATOM	1456	CG	HIS	185	3.947	4.418	38.174	1.00	12.93
ATOM	1457	CD2	HIS	185	4.013	4.381	39.527	1.00	12.64
ATOM	1458	ND1	HIS	185	2.770	5.065	37.865	1.00	12.62
ATOM	1459	CE1	HIS	185	2.155	5.412	38.981	1.00	13.67
ATOM	1460	NE2	HIS	185	2.886	5.012	40.005	1.00	12.93
ATOM	1461	C	HIS	185	5.292	2.422	35.164	1.00	13.36
ATOM	1462	O	HIS	185	6.444	1.978	35.236	1.00	13.73
ATOM	1463	N	ALA	186	4.723	2.728	34.005	1.00	12.12
ATOM	1464	CA	ALA	186	5.444	2.519	32.754	1.00	11.23
ATOM	1465	CB	ALA	186	4.494	2.722	31.587	1.00	12.26
ATOM	1466	C	ALA	186	6.677	3.422	32.541	1.00	11.54
ATOM	1467	O	ALA	186	7.739	2.964	32.104	1.00	10.68
ATOM	1468	N	GLU	187	6.530	4.698	32.855	1.00	10.75
ATOM	1469	CA	GLU	187	7.602	5.648	32.564	1.00	10.72

FIG.11B-35

ATOM	1470	CB	GLU	187	7.133	7.070	32.879	1.00	11.96
ATOM	1471	CG	GLU	187	6.042	7.443	31.817	1.00	13.69
ATOM	1472	CD	GLU	187	5.429	8.758	32.247	1.00	15.11
ATOM	1473	OE1	GLU	187	5.768	9.825	31.693	1.00	15.93
ATOM	1474	OE2	GLU	187	4.596	8.703	33.175	1.00	16.67
ATOM	1475	C	GLU	187	8.974	5.371	33.186	1.00	10.14
ATOM	1476	O	GLU	187	9.990	5.441	32.487	1.00	10.23
ATOM	1477	N	PRO	188	9.032	5.065	34.490	1.00	10.27
ATOM	1478	CD	PRO	188	7.972	5.138	35.507	1.00	10.22
ATOM	1479	CA	PRO	188	10.346	4.792	35.105	1.00	10.11
ATOM	1480	CB	PRO	188	10.013	4.656	36.610	1.00	10.75
ATOM	1481	CG	PRO	188	8.762	5.516	36.770	1.00	9.50
ATOM	1482	C	PRO	188	11.046	3.548	34.514	1.00	10.42
ATOM	1483	O	PRO	188	12.261	3.450	34.570	1.00	10.08
ATOM	1484	N	VAL	189	10.284	2.601	33.957	1.00	11.14
ATOM	1485	CA	VAL	189	10.893	1.404	33.363	1.00	10.35
ATOM	1486	CB	VAL	189	9.798	0.368	33.002	1.00	10.10
ATOM	1487	CG1	VAL	189	10.406	-0.821	32.238	1.00	10.42
ATOM	1488	CG2	VAL	189	9.118	-0.113	34.271	1.00	11.67
ATOM	1489	C	VAL	189	11.706	1.826	32.106	1.00	10.38
ATOM	1490	O	VAL	189	12.848	1.387	31.906	1.00	10.25
ATOM	1491	N	ASP	190	11.117	2.692	31.284	1.00	10.88
ATOM	1492	CA	ASP	190	11.811	3.165	30.102	1.00	10.93
ATOM	1493	CB	ASP	190	10.873	3.938	29.160	1.00	11.48
ATOM	1494	CG	ASP	190	9.993	3.059	28.286	1.00	12.68
ATOM	1495	OD1	ASP	190	10.297	1.881	28.008	1.00	12.41
ATOM	1496	OD2	ASP	190	8.958	3.577	27.818	1.00	13.13
ATOM	1497	C	ASP	190	12.991	4.064	30.512	1.00	10.81
ATOM	1498	O	ASP	190	14.032	4.050	29.855	1.00	10.56
ATOM	1499	N	VAL	191	12.850	4.818	31.603	1.00	10.14
ATOM	1500	CA	VAL	191	13.963	5.665	32.039	1.00	9.64
ATOM	1501	CB	VAL	191	13.568	6.510	33.259	1.00	9.54
ATOM	1502	CG1	VAL	191	14.815	7.130	33.895	1.00	10.40
ATOM	1503	CG2	VAL	191	12.573	7.614	32.808	1.00	10.05
ATOM	1504	C	VAL	191	15.173	4.766	32.422	1.00	9.21
ATOM	1505	O	VAL	191	16.327	5.059	32.085	1.00	9.71
ATOM	1506	N	TRP	192	14.889	3.691	33.145	1.00	9.61
ATOM	1507	CA	TRP	192	15.935	2.769	33.572	1.00	9.80
ATOM	1508	CB	TRP	192	15.321	1.662	34.439	1.00	9.06
ATOM	1509	CG	TRP	192	16.300	0.619	34.873	1.00	10.53
ATOM	1510	CD2	TRP	192	16.870	0.465	36.183	1.00	10.09
ATOM	1511	CE2	TRP	192	17.739	-0.646	36.129	1.00	10.53

FIG.11B-36

ATOM	1512	CE3	TRP	192	16.722	1.150	37.398	1.00	11.26
ATOM	1513	CD1	TRP	192	16.834	-0.371	34.105	1.00	10.22
ATOM	1514	NE1	TRP	192	17.695	-1.135	34.852	1.00	11.11
ATOM	1515	CZ2	TRP	192	18.466	-1.091	37.245	1.00	11.96
ATOM	1516	CZ3	TRP	192	17.442	0.703	38.514	1.00	11.54
ATOM	1517	CH2	TRP	192	18.305	-0.409	38.421	1.00	10.99
ATOM	1518	C	TRP	192	16.684	2.150	32.394	1.00	9.91
ATOM	1519	O	TRP	192	17.927	2.133	32.389	1.00	9.89
ATOM	1520	N	SER	193	15.949	1.619	31.412	1.00	9.48
ATOM	1521	CA	SER	193	16.618	1.031	30.253	1.00	9.06
ATOM	1522	CB	SER	193	15.610	0.363	29.307	1.00	9.01
ATOM	1523	OG	SER	193	14.587	1.257	28.916	1.00	11.65
ATOM	1524	C	SER	193	17.463	2.104	29.510	1.00	9.89
ATOM	1525	O	SER	193	18.520	1.780	28.967	1.00	9.64
ATOM	1526	N	CYS	194	16.999	3.356	29.479	1.00	9.70
ATOM	1527	CA	CYS	194	17.796	4.415	28.847	1.00	9.62
ATOM	1528	CB	CYS	194	17.061	5.766	28.851	1.00	9.27
ATOM	1529	SG	CYS	194	15.742	5.746	27.560	1.00	12.52
ATOM	1530	C	CYS	194	19.151	4.594	29.654	1.00	9.45
ATOM	1531	O	CYS	194	20.178	4.902	29.068	1.00	9.86
ATOM	1532	N	GLY	195	19.104	4.380	30.965	1.00	9.58
ATOM	1533	CA	GLY	195	20.307	4.477	31.793	1.00	9.44
ATOM	1534	C	GLY	195	21.288	3.352	31.471	1.00	10.40
ATOM	1535	O	GLY	195	22.498	3.555	31.435	1.00	10.09
ATOM	1536	N	ILE	196	20.762	2.156	31.232	1.00	10.86
ATOM	1537	CA	ILE	196	21.631	1.023	30.897	1.00	12.49
ATOM	1538	CB	ILE	196	20.823	-0.290	30.971	1.00	13.21
ATOM	1539	CG2	ILE	196	19.584	-0.159	30.189	1.00	18.11
ATOM	1540	CG1	ILE	196	21.610	-1.452	30.371	1.00	14.47
ATOM	1541	CD1	ILE	196	22.737	-1.828	31.133	1.00	18.68
ATOM	1542	C	ILE	196	22.249	1.273	29.493	1.00	11.39
ATOM	1543	O	ILE	196	23.409	0.928	29.249	1.00	11.50
ATOM	1544	N	VAL	197	21.476	1.887	28.592	1.00	10.64
ATOM	1545	CA	VAL	197	21.989	2.198	27.257	1.00	9.96
ATOM	1546	CB	VAL	197	20.868	2.778	26.358	1.00	9.29
ATOM	1547	CG1	VAL	197	21.465	3.425	25.088	1.00	10.47
ATOM	1548	CG2	VAL	197	19.911	1.637	25.963	1.00	10.17
ATOM	1549	C	VAL	197	23.129	3.209	27.398	1.00	10.49
ATOM	1550	O	VAL	197	24.161	3.108	26.726	1.00	10.94
ATOM	1551	N	LEU	198	22.944	4.178	28.292	1.00	10.69
ATOM	1552	CA	LEU	198	23.977	5.194	28.517	1.00	11.25
ATOM	1553	CB	LEU	198	23.537	6.200	29.571	1.00	12.55

FIG.11B-37

ATOM	1554	CG	LEU	198	23.879	7.664	29.261	1.00	16.51
ATOM	1555	CD1	LEU	198	23.869	8.361	30.615	1.00	12.50
ATOM	1556	CD2	LEU	198	25.154	7.918	28.500	1.00	13.83
ATOM	1557	C	LEU	198	25.253	4.511	29.047	1.00	11.79
ATOM	1558	O	LEU	198	26.371	4.801	28.600	1.00	11.82
ATOM	1559	N	THR	199	25.067	3.592	29.985	1.00	11.20
ATOM	1560	CA	THR	199	26.199	2.862	30.574	1.00	11.87
ATOM	1561	CB	THR	199	25.699	1.860	31.641	1.00	11.32
ATOM	1562	OG1	THR	199	25.041	2.585	32.677	1.00	11.23
ATOM	1563	CG2	THR	199	26.878	1.088	32.291	1.00	11.31
ATOM	1564	C	THR	199	26.947	2.154	29.486	1.00	12.08
ATOM	1565	O	THR	199	28.181	2.237	29.410	1.00	12.74
ATOM	1566	N	ALA	200	26.202	1.474	28.614	1.00	13.09
ATOM	1567	CA	ALA	200	26.805	0.737	27.506	1.00	13.17
ATOM	1568	CB	ALA	200	25.720	0.002	26.712	1.00	12.95
ATOM	1569	C	ALA	200	27.589	1.668	26.568	1.00	14.04
ATOM	1570	O	ALA	200	28.690	1.345	26.140	1.00	13.51
ATOM	1571	N	MET	201	27.023	2.822	26.241	1.00	12.86
ATOM	1572	CA	MET	201	27.725	3.728	25.335	1.00	12.63
ATOM	1573	CB	MET	201	26.849	4.930	24.954	1.00	12.56
ATOM	1574	CG	MET	201	25.592	4.544	24.110	1.00	13.61
ATOM	1575	SD	MET	201	24.831	6.026	23.390	1.00	12.69
ATOM	1576	CE	MET	201	24.080	6.854	24.850	1.00	12.19
ATOM	1577	C	MET	201	29.011	4.268	25.933	1.00	12.12
ATOM	1578	O	MET	201	29.997	4.484	25.222	1.00	12.45
ATOM	1579	N	LEU	202	29.019	4.458	27.247	1.00	11.16
ATOM	1580	CA	LEU	202	30.199	5.014	27.907	1.00	12.42
ATOM	1581	CB	LEU	202	29.782	5.864	29.110	1.00	12.19
ATOM	1582	CG	LEU	202	28.994	7.113	28.691	1.00	11.96
ATOM	1583	CD1	LEU	202	28.551	7.912	29.931	1.00	13.07
ATOM	1584	CD2	LEU	202	29.891	7.960	27.796	1.00	12.51
ATOM	1585	C	LEU	202	31.262	4.003	28.384	1.00	13.40
ATOM	1586	O	LEU	202	32.414	4.384	28.610	1.00	14.80
ATOM	1587	N	ALA	203	30.893	2.734	28.514	1.00	13.10
ATOM	1588	CA	ALA	203	31.839	1.726	28.988	1.00	15.17
ATOM	1589	CB	ALA	203	31.424	1.252	30.367	1.00	14.79
ATOM	1590	C	ALA	203	32.004	0.521	28.047	1.00	15.81
ATOM	1591	O	ALA	203	32.926	-0.290	28.216	1.00	17.03
ATOM	1592	N	GLY	204	31.117	0.394	27.070	1.00	15.77
ATOM	1593	CA	GLY	204	31.218	-0.728	26.149	1.00	17.71
ATOM	1594	C	GLY	204	30.957	-2.072	26.803	1.00	18.37
ATOM	1595	O	GLY	204	31.451	-3.112	26.340	1.00	19.10

FIG.11B-38

ATOM	1596	N	GLU	205	30.199	-2.052	27.888	1.00	18.22
ATOM	1597	CA	GLU	205	29.850	-3.268	28.610	1.00	19.72
ATOM	1598	CB	GLU	205	30.977	-3.692	29.552	1.00	22.13
ATOM	1599	CG	GLU	205	31.134	-3.004	30.896	1.00	24.83
ATOM	1600	CD	GLU	205	32.225	-3.740	31.729	1.00	25.92
ATOM	1601	OE1	GLU	205	32.102	-4.890	32.202	1.00	28.12
ATOM	1602	OE2	GLU	205	33.274	-3.121	31.912	1.00	26.08
ATOM	1603	C	GLU	205	28.582	-3.039	29.424	1.00	18.53
ATOM	1604	O	GLU	205	28.292	-1.915	29.845	1.00	18.22
ATOM	1605	N	LEU	206	27.819	-4.107	29.622	1.00	17.56
ATOM	1606	CA	LEU	206	26.579	-4.045	30.396	1.00	17.14
ATOM	1607	CB	LEU	206	25.563	-5.054	29.847	1.00	17.00
ATOM	1608	CG	LEU	206	25.030	-4.728	28.447	1.00	18.03
ATOM	1609	CD1	LEU	206	26.152	-4.419	27.471	1.00	22.13
ATOM	1610	CD2	LEU	206	24.233	-5.927	27.948	1.00	17.79
ATOM	1611	C	LEU	206	26.976	-4.351	31.811	1.00	16.84
ATOM	1612	O	LEU	206	27.782	-5.263	32.057	1.00	16.85
ATOM	1613	N	PRO	207	26.420	-3.604	32.777	1.00	16.25
ATOM	1614	CD	PRO	207	25.415	-2.545	32.548	1.00	15.91
ATOM	1615	CA	PRO	207	26.712	-3.757	34.209	1.00	16.93
ATOM	1616	CB	PRO	207	26.077	-2.503	34.816	1.00	16.06
ATOM	1617	CG	PRO	207	24.870	-2.295	33.934	1.00	15.81
ATOM	1618	C	PRO	207	26.305	-5.042	34.871	1.00	17.01
ATOM	1619	O	PRO	207	27.012	-5.518	35.767	1.00	17.85
ATOM	1620	N	TRP	208	25.181	-5.626	34.454	1.00	16.29
ATOM	1621	CA	TRP	208	24.726	-6.868	35.074	1.00	16.75
ATOM	1622	CB	TRP	208	24.006	-6.564	36.392	1.00	16.28
ATOM	1623	CG	TRP	208	23.028	-5.406	36.304	1.00	15.34
ATOM	1624	CD2	TRP	208	23.198	-4.109	36.880	1.00	15.76
ATOM	1625	CE2	TRP	208	22.085	-3.323	36.492	1.00	14.77
ATOM	1626	CE3	TRP	208	24.186	-3.530	37.686	1.00	14.76
ATOM	1627	CD1	TRP	208	21.843	-5.365	35.608	1.00	15.76
ATOM	1628	NE1	TRP	208	21.273	-4.112	35.717	1.00	15.54
ATOM	1629	CZ2	TRP	208	21.935	-1.991	36.882	1.00	14.39
ATOM	1630	CZ3	TRP	208	24.037	-2.206	38.078	1.00	15.33
ATOM	1631	CH2	TRP	208	22.915	-1.445	37.674	1.00	14.72
ATOM	1632	C	TRP	208	23.801	-7.720	34.202	1.00	17.33
ATOM	1633	O	TRP	208	23.167	-7.214	33.270	1.00	17.29
ATOM	1634	N	ASP	209	23.739	-9.013	34.514	1.00	18.37
ATOM	1635	CA	ASP	209	22.885	-9.953	33.786	1.00	18.97
ATOM	1636	CB	ASP	209	23.083	-11.397	34.282	1.00	22.30
ATOM	1637	CG	ASP	209	24.466	-11.974	34.039	1.00	23.93

FIG.11B-39

ATOM	1638	OD1	ASP	209	25.057	-11.638	32.994	1.00	25.16
ATOM	1639	OD2	ASP	209	24.939	-12.771	34.884	1.00	27.15
ATOM	1640	C	ASP	209	21.406	-9.587	33.984	1.00	18.77
ATOM	1641	O	ASP	209	20.604	-9.675	33.052	1.00	17.74
ATOM	1642	N	GLN	210	21.068	-9.178	35.205	1.00	18.55
ATOM	1643	CA	GLN	210	19.712	-8.775	35.559	1.00	19.19
ATOM	1644	CB	GLN	210	18.805	-10.003	35.664	1.00	20.25
ATOM	1645	CG	GLN	210	19.377	-11.006	36.658	1.00	21.64
ATOM	1646	CD	GLN	210	18.489	-12.229	36.576	1.00	23.03
ATOM	1647	OE1	GLN	210	18.452	-12.918	35.555	1.00	23.31
ATOM	1648	NE2	GLN	210	17.765	-12.503	37.650	1.00	24.19
ATOM	1649	C	GLN	210	19.775	-8.010	36.865	1.00	19.59
ATOM	1650	O	GLN	210	20.691	-8.209	37.669	1.00	18.71
ATOM	1651	N	PRO	211	18.806	-7.111	37.105	1.00	18.57
ATOM	1652	CD	PRO	211	17.799	-6.619	36.150	1.00	18.07
ATOM	1653	CA	PRO	211	18.783	-6.311	38.334	1.00	19.80
ATOM	1654	CB	PRO	211	17.999	-5.071	37.895	1.00	19.10
ATOM	1655	CG	PRO	211	16.995	-5.644	37.004	1.00	18.49
ATOM	1656	C	PRO	211	18.202	-7.039	39.533	1.00	21.25
ATOM	1657	O	PRO	211	17.149	-6.664	40.049	1.00	20.53
ATOM	1658	N	SER	212	18.914	-8.068	39.986	1.00	22.92
ATOM	1659	CA	SER	212	18.476	-8.876	41.122	1.00	25.26
ATOM	1660	CB	SER	212	18.232	-10.322	40.696	1.00	25.71
ATOM	1661	OG	SER	212	17.269	-10.404	39.656	1.00	27.04
ATOM	1662	C	SER	212	19.540	-8.909	42.200	1.00	26.27
ATOM	1663	O	SER	212	20.728	-8.823	41.911	1.00	26.27
ATOM	1664	N	ASP	213	19.112	-9.031	43.449	1.00	28.30
ATOM	1665	CA	ASP	213	20.060	-9.091	44.558	1.00	30.12
ATOM	1666	CB	ASP	213	19.308	-9.155	45.885	1.00	31.41
ATOM	1667	CG	ASP	213	18.700	-7.785	46.123	1.00	32.87
ATOM	1668	OD1	ASP	213	17.794	-7.695	46.971	1.00	34.35
ATOM	1669	OD2	ASP	213	19.131	-6.806	45.478	1.00	33.85
ATOM	1670	C	ASP	213	20.950	-10.325	44.402	1.00	30.47
ATOM	1671	O	ASP	213	22.085	-10.347	44.881	1.00	30.66
ATOM	1672	N	SER	214	20.431	-11.345	43.722	1.00	30.65
ATOM	1673	CA	SER	214	21.182	-12.577	43.493	1.00	30.71
ATOM	1674	CB	SER	214	20.266	-13.676	42.955	1.00	31.27
ATOM	1675	OG	SER	214	19.713	-13.315	41.699	1.00	33.24
ATOM	1676	C	SER	214	22.295	-12.353	42.480	1.00	30.15
ATOM	1677	O	SER	214	23.180	-13.201	42.301	1.00	30.59
ATOM	1678	N	CYS	215	22.237	-11.212	41.802	1.00	28.37
ATOM	1679	CA	CYS	215	23.248	-10.857	40.817	1.00	27.11

FIG.11B-40

ATOM	1680	CB	CYS	215	22.615	-10.052	39.679	1.00	27.35
ATOM	1681	SG	CYS	215	23.795	-9.692	38.381	1.00	24.98
ATOM	1682	C	CYS	215	24.290	-10.029	41.524	1.00	26.85
ATOM	1683	O	CYS	215	24.046	-8.879	41.881	1.00	25.26
ATOM	1684	N	GLN	216	25.465	-10.618	41.730	1.00	26.11
ATOM	1685	CA	GLN	216	26.547	-9.945	42.432	1.00	25.73
ATOM	1686	CB	GLN	216	27.806	-10.824	42.396	1.00	27.39
ATOM	1687	CG	GLN	216	28.908	-10.267	43.303	1.00	29.33
ATOM	1688	CD	GLN	216	28.445	-10.161	44.773	1.00	30.23
ATOM	1689	OE1	GLN	216	28.777	-9.201	45.469	1.00	31.39
ATOM	1690	NE2	GLN	216	27.691	-11.153	45.236	1.00	29.72
ATOM	1691	C	GLN	216	26.867	-8.526	41.914	1.00	24.91
ATOM	1692	O	GLN	216	27.064	-7.606	42.705	1.00	24.59
ATOM	1693	N	GLU	217	26.904	-8.356	40.597	1.00	23.79
ATOM	1694	CA	GLU	217	27.214	-7.054	40.015	1.00	22.82
ATOM	1695	CB	GLU	217	27.325	-7.161	38.490	1.00	23.60
ATOM	1696	CG	GLU	217	28.545	-7.945	37.893	1.00	25.50
ATOM	1697	CD	GLU	217	28.552	-9.382	38.379	1.00	26.01
ATOM	1698	OE1	GLU	217	27.461	-9.984	38.421	1.00	26.36
ATOM	1699	OE2	GLU	217	29.642	-9.904	38.709	1.00	27.79
ATOM	1700	C	GLU	217	26.168	-6.008	40.387	1.00	22.40
ATOM	1701	O	GLU	217	26.494	-4.833	40.597	1.00	21.57
ATOM	1702	N	TYR	218	24.909	-6.430	40.467	1.00	21.63
ATOM	1703	CA	TYR	218	23.854	-5.496	40.834	1.00	21.45
ATOM	1704	CB	TYR	218	22.469	-6.076	40.518	1.00	20.94
ATOM	1705	CG	TYR	218	21.349	-5.103	40.821	1.00	20.26
ATOM	1706	CD1	TYR	218	21.289	-3.860	40.185	1.00	20.20
ATOM	1707	CE1	TYR	218	20.290	-2.943	40.488	1.00	19.98
ATOM	1708	CD2	TYR	218	20.371	-5.401	41.769	1.00	20.62
ATOM	1709	CE2	TYR	218	19.371	-4.492	42.081	1.00	20.13
ATOM	1710	CZ	TYR	218	19.336	-3.263	41.436	1.00	19.91
ATOM	1711	OH	TYR	218	18.345	-2.359	41.727	1.00	20.57
ATOM	1712	C	TYR	218	23.988	-5.145	42.332	1.00	22.12
ATOM	1713	O	TYR	218	23.853	-3.988	42.706	1.00	21.46
ATOM	1714	N	SER	219	24.261	-6.139	43.178	1.00	22.64
ATOM	1715	CA	SER	219	24.423	-5.854	44.605	1.00	23.55
ATOM	1716	CB	SER	219	24.738	-7.128	45.403	1.00	24.17
ATOM	1717	OG	SER	219	23.642	-8.018	45.381	1.00	26.99
ATOM	1718	C	SER	219	25.580	-4.878	44.801	1.00	23.48
ATOM	1719	O	SER	219	25.481	-3.930	45.578	1.00	24.10
ATOM	1720	N	ASP	220	26.673	-5.109	44.082	1.00	23.52
ATOM	1721	CA	ASP	220	27.837	-4.240	44.169	1.00	22.96

FIG.11B-41

ATOM	1722	CB	ASP	220	28.941	-4.732	43.232	1.00	24.39
ATOM	1723	CG	ASP	220	29.580	-5.983	43.835	1.00	25.92
ATOM	1724	OD1	ASP	220	30.398	-6.603	43.128	1.00	28.41
ATOM	1725	OD2	ASP	220	29.278	-6.340	44.992	1.00	27.22
ATOM	1726	C	ASP	220	27.480	-2.786	43.828	1.00	22.40
ATOM	1727	O	ASP	220	28.005	-1.855	44.428	1.00	22.30
ATOM	1728	N	TRP	221	26.585	-2.594	42.865	1.00	21.17
ATOM	1729	CA	TRP	221	26.179	-1.241	42.498	1.00	20.70
ATOM	1730	CB	TRP	221	25.391	-1.291	41.176	1.00	19.27
ATOM	1731	CG	TRP	221	24.638	-0.020	40.833	1.00	17.73
ATOM	1732	CD2	TRP	221	25.191	1.230	40.395	1.00	16.84
ATOM	1733	CE2	TRP	221	24.106	2.117	40.187	1.00	17.43
ATOM	1734	CE3	TRP	221	26.491	1.688	40.154	1.00	17.01
ATOM	1735	CD1	TRP	221	23.287	0.156	40.874	1.00	17.87
ATOM	1736	NE1	TRP	221	22.959	1.435	40.491	1.00	17.27
ATOM	1737	CZ2	TRP	221	24.284	3.438	39.747	1.00	16.90
ATOM	1738	CZ3	TRP	221	26.668	3.013	39.715	1.00	16.65
ATOM	1739	CH2	TRP	221	25.573	3.864	39.518	1.00	17.11
ATOM	1740	C	TRP	221	25.376	-0.599	43.651	1.00	21.75
ATOM	1741	O	TRP	221	25.617	0.552	44.015	1.00	21.20
ATOM	1742	N	LYS	222	24.441	-1.351	44.225	1.00	23.83
ATOM	1743	CA	LYS	222	23.641	-0.828	45.324	1.00	26.15
ATOM	1744	CB	LYS	222	22.564	-1.831	45.735	1.00	26.74
ATOM	1745	CG	LYS	222	21.471	-1.821	44.636	1.00	27.05
ATOM	1746	CD	LYS	222	20.119	-2.467	45.022	1.00	28.62
ATOM	1747	CE	LYS	222	20.199	-3.943	45.413	1.00	28.17
ATOM	1748	NZ	LYS	222	18.869	-4.443	45.862	1.00	30.18
ATOM	1749	C	LYS	222	24.524	-0.497	46.528	1.00	27.58
ATOM	1750	O	LYS	222	24.150	0.320	47.371	1.00	27.87
ATOM	1751	N	GLU	223	25.694	-1.126	46.586	1.00	29.19
ATOM	1752	CA	GLU	223	26.650	-0.902	47.670	1.00	30.71
ATOM	1753	CB	GLU	223	27.426	-2.187	47.975	1.00	32.35
ATOM	1754	CG	GLU	223	26.514	-3.389	48.320	1.00	35.04
ATOM	1755	CD	GLU	223	27.341	-4.629	48.610	1.00	36.39
ATOM	1756	OE1	GLU	223	28.026	-4.647	49.652	1.00	37.89
ATOM	1757	OE2	GLU	223	27.315	-5.583	47.799	1.00	38.16
ATOM	1758	C	GLU	223	27.641	0.207	47.299	1.00	31.11
ATOM	1759	O	GLU	223	28.595	0.476	48.035	1.00	31.11
ATOM	1760	N	LYS	224	27.414	0.835	46.147	1.00	31.36
ATOM	1761	CA	LYS	224	28.250	1.935	45.669	1.00	31.60
ATOM	1762	CB	LYS	224	28.250	3.084	46.683	1.00	32.70
ATOM	1763	CG	LYS	224	26.902	3.828	46.813	1.00	34.17

FIG.11B-42

ATOM	1764	CD	LYS	224	25.731	2.967	47.318	1.00	35.15
ATOM	1765	CE	LYS	224	25.845	2.601	48.823	1.00	36.31
ATOM	1766	NZ	LYS	224	25.781	3.822	49.677	1.00	37.18
ATOM	1767	C	LYS	224	29.720	1.607	45.343	1.00	31.34
ATOM	1768	O	LYS	224	30.595	2.467	45.463	1.00	31.10
ATOM	1769	N	LYS	225	29.982	0.377	44.918	1.00	30.93
ATOM	1770	CA	LYS	225	31.347	-0.028	44.574	1.00	31.37
ATOM	1771	CB	LYS	225	31.493	-1.543	44.742	1.00	31.69
ATOM	1772	CG	LYS	225	31.227	-1.904	46.232	1.00	32.87
ATOM	1773	CD	LYS	225	31.162	-3.409	46.591	1.00	33.45
ATOM	1774	CE	LYS	225	32.345	-4.339	46.300	1.00	35.03
ATOM	1775	NZ	LYS	225	32.064	-5.731	46.759	1.00	36.16
ATOM	1776	C	LYS	225	31.641	0.382	43.114	1.00	30.98
ATOM	1777	O	LYS	225	31.751	-0.465	42.230	1.00	30.71
ATOM	1778	N	THR	226	31.766	1.685	42.886	1.00	31.21
ATOM	1779	CA	THR	226	32.009	2.208	41.546	1.00	31.56
ATOM	1780	CB	THR	226	31.458	3.659	41.422	1.00	31.65
ATOM	1781	OG1	THR	226	31.977	4.479	42.478	1.00	32.08
ATOM	1782	CG2	THR	226	29.939	3.650	41.514	1.00	31.20
ATOM	1783	C	THR	226	33.464	2.137	41.108	1.00	31.92
ATOM	1784	O	THR	226	33.869	2.803	40.155	1.00	32.06
ATOM	1785	N	TYR	227	34.252	1.326	41.807	1.00	32.46
ATOM	1786	CA	TYR	227	35.653	1.151	41.456	1.00	32.59
ATOM	1787	CB	TYR	227	36.518	1.115	42.724	1.00	33.51
ATOM	1788	CG	TYR	227	36.011	0.186	43.801	1.00	34.46
ATOM	1789	CD1	TYR	227	36.185	-1.196	43.703	1.00	35.44
ATOM	1790	CE1	TYR	227	35.714	-2.052	44.699	1.00	35.37
ATOM	1791	CD2	TYR	227	35.351	0.691	44.920	1.00	34.76
ATOM	1792	CE2	TYR	227	34.874	-0.154	45.917	1.00	35.15
ATOM	1793	CZ	TYR	227	35.058	-1.521	45.802	1.00	35.04
ATOM	1794	OH	TYR	227	34.576	-2.348	46.791	1.00	35.61
ATOM	1795	C	TYR	227	35.762	-0.135	40.664	1.00	32.78
ATOM	1796	O	TYR	227	36.852	-0.539	40.254	1.00	32.53
ATOM	1797	N	LEU	228	34.614	-0.779	40.464	1.00	32.64
ATOM	1798	CA	LEU	228	34.517	-2.022	39.709	1.00	33.70
ATOM	1799	CB	LEU	228	33.390	-2.897	40.261	1.00	33.23
ATOM	1800	CG	LEU	228	33.791	-3.328	41.675	1.00	33.68
ATOM	1801	CD1	LEU	228	32.676	-4.197	42.238	1.00	33.31
ATOM	1802	CD2	LEU	228	35.116	-4.095	41.668	1.00	33.11
ATOM	1803	C	LEU	228	34.264	-1.734	38.222	1.00	34.23
ATOM	1804	O	LEU	228	33.627	-0.743	37.874	1.00	34.83
ATOM	1805	N	ASN	229	34.762	-2.640	37.387	1.00	35.26

FIG.11B-43

ATOM	1806	CA	ASN	229	34.716	-2.588	35.925	1.00	35.58
ATOM	1807	CB	ASN	229	34.458	-3.987	35.346	1.00	36.34
ATOM	1808	CG	ASN	229	35.512	-4.243	34.249	1.00	37.55
ATOM	1809	OD1	ASN	229	36.703	-4.002	34.455	1.00	37.91
ATOM	1810	ND2	ASN	229	35.069	-4.742	33.096	1.00	37.37
ATOM	1811	C	ASN	229	33.829	-1.633	35.198	1.00	34.28
ATOM	1812	O	ASN	229	34.300	-0.626	34.665	1.00	35.89
ATOM	1813	N	PRO	230	32.516	-1.897	35.159	1.00	33.61
ATOM	1814	CD	PRO	230	31.668	-2.722	36.038	1.00	32.77
ATOM	1815	CA	PRO	230	31.718	-0.924	34.408	1.00	30.57
ATOM	1816	CB	PRO	230	30.287	-1.447	34.623	1.00	32.30
ATOM	1817	CG	PRO	230	30.340	-1.971	36.006	1.00	33.38
ATOM	1818	C	PRO	230	31.960	0.575	34.781	1.00	27.81
ATOM	1819	O	PRO	230	32.499	1.367	33.990	1.00	26.92
ATOM	1820	N	TRP	231	31.578	0.918	35.999	1.00	24.76
ATOM	1821	CA	TRP	231	31.652	2.276	36.514	1.00	22.97
ATOM	1822	CB	TRP	231	30.995	2.295	37.899	1.00	21.67
ATOM	1823	CG	TRP	231	29.833	1.331	37.961	1.00	19.36
ATOM	1824	CD2	TRP	231	28.622	1.407	37.204	1.00	18.86
ATOM	1825	CE2	TRP	231	27.878	0.239	37.485	1.00	18.66
ATOM	1826	CE3	TRP	231	28.095	2.350	36.310	1.00	17.74
ATOM	1827	CD1	TRP	231	29.773	0.155	38.660	1.00	19.31
ATOM	1828	NE1	TRP	231	28.605	-0.509	38.377	1.00	17.81
ATOM	1829	CZ2	TRP	231	26.634	-0.012	36.904	1.00	17.32
ATOM	1830	CZ3	TRP	231	26.856	2.103	35.727	1.00	18.02
ATOM	1831	CH2	TRP	231	26.139	0.928	36.031	1.00	17.78
ATOM	1832	C	TRP	231	33.033	2.946	36.558	1.00	22.63
ATOM	1833	O	TRP	231	33.128	4.159	36.415	1.00	22.81
ATOM	1834	N	LYS	232	34.091	2.170	36.754	1.00	22.60
ATOM	1835	CA	LYS	232	35.428	2.764	36.826	1.00	22.75
ATOM	1836	CB	LYS	232	36.477	1.704	37.189	1.00	24.11
ATOM	1837	CG	LYS	232	36.647	0.419	36.346	1.00	25.74
ATOM	1838	CD	LYS	232	37.683	-0.509	37.036	1.00	27.06
ATOM	1839	CE	LYS	232	37.996	-1.774	36.213	1.00	27.57
ATOM	1840	NZ	LYS	232	39.033	-2.612	36.876	1.00	28.69
ATOM	1841	C	LYS	232	35.860	3.438	35.529	1.00	22.63
ATOM	1842	O	LYS	232	36.790	4.258	35.522	1.00	22.71
ATOM	1843	N	LYS	233	35.182	3.104	34.435	1.00	20.74
ATOM	1844	CA	LYS	233	35.522	3.658	33.122	1.00	20.06
ATOM	1845	CB	LYS	233	35.264	2.634	32.011	1.00	21.41
ATOM	1846	CG	LYS	233	36.100	1.349	32.118	1.00	22.20
ATOM	1847	CD	LYS	233	35.874	0.176	31.106	1.00	23.44

FIG.11B-44

ATOM	1848	CE	LYS	233	34.596	-0.617	31.187	1.00	24.11
ATOM	1849	NZ	LYS	233	34.558	-1.720	30.177	1.00	24.50
ATOM	1850	C	LYS	233	34.855	5.008	32.889	1.00	19.90
ATOM	1851	O	LYS	233	35.272	5.662	31.949	1.00	18.76
ATOM	1852	N	ILE	234	33.741	5.339	33.521	1.00	20.48
ATOM	1853	CA	ILE	234	32.935	6.424	32.978	1.00	21.37
ATOM	1854	CB	ILE	234	31.491	6.107	33.470	1.00	20.52
ATOM	1855	CG2	ILE	234	30.511	7.217	33.130	1.00	20.33
ATOM	1856	CG1	ILE	234	31.126	4.755	32.836	1.00	19.24
ATOM	1857	CD1	ILE	234	29.665	4.267	33.021	1.00	18.12
ATOM	1858	C	ILE	234	33.591	7.883	33.073	1.00	23.34
ATOM	1859	O	ILE	234	34.414	8.250	32.223	1.00	26.22
ATOM	1860	N	ASP	235	33.190	8.659	34.058	1.00	23.93
ATOM	1861	CA	ASP	235	33.700	10.001	34.367	1.00	21.53
ATOM	1862	CB	ASP	235	33.670	10.978	33.182	1.00	23.07
ATOM	1863	CG	ASP	235	34.063	12.339	33.827	1.00	24.23
ATOM	1864	OD1	ASP	235	33.209	13.262	33.921	1.00	23.91
ATOM	1865	OD2	ASP	235	35.237	12.473	34.266	1.00	23.71
ATOM	1866	C	ASP	235	32.742	10.372	35.366	1.00	21.02
ATOM	1867	O	ASP	235	31.577	10.002	35.253	1.00	18.48
ATOM	1868	N	SER	236	33.180	11.101	36.387	1.00	20.18
ATOM	1869	CA	SER	236	32.301	11.481	37.480	1.00	20.49
ATOM	1870	CB	SER	236	33.036	12.390	38.481	1.00	21.41
ATOM	1871	OG	SER	236	33.526	13.563	37.863	1.00	23.42
ATOM	1872	C	SER	236	30.995	12.139	37.117	1.00	18.82
ATOM	1873	O	SER	236	29.971	11.832	37.730	1.00	18.56
ATOM	1874	N	ALA	237	31.019	13.033	36.129	1.00	18.12
ATOM	1875	CA	ALA	237	29.825	13.764	35.701	1.00	16.44
ATOM	1876	CB	ALA	237	30.194	14.812	34.635	1.00	16.94
ATOM	1877	C	ALA	237	28.709	12.817	35.170	1.00	15.31
ATOM	1878	O	ALA	237	27.590	12.819	35.691	1.00	15.03
ATOM	1879	N	PRO	238	28.991	12.040	34.116	1.00	14.33
ATOM	1880	CD	PRO	238	30.153	11.960	33.207	1.00	13.45
ATOM	1881	CA	PRO	238	27.908	11.156	33.665	1.00	13.64
ATOM	1882	CB	PRO	238	28.424	10.619	32.335	1.00	12.66
ATOM	1883	CG	PRO	238	29.934	10.623	32.526	1.00	13.78
ATOM	1884	C	PRO	238	27.584	10.063	34.714	1.00	13.32
ATOM	1885	O	PRO	238	26.461	9.578	34.799	1.00	13.46
ATOM	1886	N	LEU	239	28.579	9.686	35.509	1.00	14.55
ATOM	1887	CA	LEU	239	28.363	8.677	36.530	1.00	14.31
ATOM	1888	CB	LEU	239	29.702	8.330	37.192	1.00	15.38
ATOM	1889	CG	LEU	239	29.797	7.069	38.059	1.00	17.03

FIG.11B-45

ATOM	1890	CD1	LEU	239	29.461	7.543	39.426	1.00	19.97
ATOM	1891	CD2	LEU	239	28.941	5.890	37.632	1.00	16.99
ATOM	1892	C	LEU	239	27.350	9.209	37.548	1.00	14.32
ATOM	1893	O	LEU	239	26.521	8.451	38.053	1.00	13.88
ATOM	1894	N	ALA	240	27.410	10.513	37.836	1.00	13.60
ATOM	1895	CA	ALA	240	26.474	11.121	38.778	1.00	14.03
ATOM	1896	CB	ALA	240	26.834	12.596	39.042	1.00	14.41
ATOM	1897	C	ALA	240	25.049	11.017	38.214	1.00	13.80
ATOM	1898	O	ALA	240	24.105	10.815	38.959	1.00	15.01
ATOM	1899	N	LEU	241	24.911	11.141	36.898	1.00	13.56
ATOM	1900	CA	LEU	241	23.586	11.029	36.289	1.00	12.69
ATOM	1901	CB	LEU	241	23.612	11.492	34.824	1.00	12.29
ATOM	1902	CG	LEU	241	22.307	11.217	34.050	1.00	12.22
ATOM	1903	CD1	LEU	241	21.101	11.892	34.673	1.00	13.19
ATOM	1904	CD2	LEU	241	22.521	11.700	32.616	1.00	11.55
ATOM	1905	C	LEU	241	23.144	9.585	36.389	1.00	12.74
ATOM	1906	O	LEU	241	21.992	9.298	36.744	1.00	13.22
ATOM	1907	N	LEU	242	24.051	8.658	36.086	1.00	12.48
ATOM	1908	CA	LEU	242	23.697	7.242	36.165	1.00	13.46
ATOM	1909	CB	LEU	242	24.901	6.395	35.710	1.00	14.09
ATOM	1910	CG	LEU	242	24.951	5.527	34.437	1.00	17.22
ATOM	1911	CD1	LEU	242	23.861	5.790	33.451	1.00	13.60
ATOM	1912	CD2	LEU	242	26.335	5.691	33.831	1.00	14.06
ATOM	1913	C	LEU	242	23.256	6.879	37.622	1.00	13.59
ATOM	1914	O	LEU	242	22.369	6.034	37.834	1.00	13.32
ATOM	1915	N	HIS	243	23.861	7.526	38.615	1.00	14.11
ATOM	1916	CA	HIS	243	23.485	7.251	40.004	1.00	14.54
ATOM	1917	CB	HIS	243	24.385	8.001	40.998	1.00	16.02
ATOM	1918	CG	HIS	243	25.597	7.228	41.426	1.00	18.57
ATOM	1919	CD2	HIS	243	26.911	7.424	41.173	1.00	20.62
ATOM	1920	ND1	HIS	243	25.524	6.099	42.216	1.00	20.36
ATOM	1921	CE1	HIS	243	26.743	5.632	42.427	1.00	19.94
ATOM	1922	NE2	HIS	243	27.603	6.418	41.804	1.00	20.07
ATOM	1923	C	HIS	243	22.037	7.679	40.279	1.00	14.42
ATOM	1924	O	HIS	243	21.400	7.148	41.181	1.00	15.58
ATOM	1925	N	LYS	244	21.548	8.652	39.513	1.00	13.04
ATOM	1926	CA	LYS	244	20.181	9.138	39.662	1.00	12.66
ATOM	1927	CB	LYS	244	20.061	10.586	39.215	1.00	13.26
ATOM	1928	CG	LYS	244	20.819	11.500	40.245	1.00	13.78
ATOM	1929	CD	LYS	244	20.709	12.997	39.911	1.00	16.39
ATOM	1930	CE	LYS	244	21.462	13.451	38.618	1.00	16.70
ATOM	1931	NZ	LYS	244	21.476	14.962	38.449	1.00	17.30

FIG.11B-46

ATOM	1932	C	LYS	244	19.164	8.319	38.858	1.00	12.13
ATOM	1933	O	LYS	244	17.993	8.241	39.224	1.00	12.40
ATOM	1934	N	ILE	245	19.621	7.723	37.759	1.00	12.05
ATOM	1935	CA	ILE	245	18.747	6.906	36.912	1.00	10.91
ATOM	1936	CB	ILE	245	19.281	6.819	35.449	1.00	10.95
ATOM	1937	CG2	ILE	245	18.405	5.864	34.617	1.00	10.91
ATOM	1938	CG1	ILE	245	19.237	8.197	34.786	1.00	11.13
ATOM	1939	CD1	ILE	245	19.900	8.235	33.354	1.00	12.03
ATOM	1940	C	ILE	245	18.606	5.451	37.419	1.00	12.05
ATOM	1941	O	ILE	245	17.502	4.913	37.489	1.00	13.24
ATOM	1942	N	LEU	246	19.726	4.831	37.777	1.00	12.15
ATOM	1943	CA	LEU	246	19.715	3.436	38.208	1.00	12.12
ATOM	1944	CB	LEU	246	21.025	2.757	37.761	1.00	11.77
ATOM	1945	CG	LEU	246	21.265	2.878	36.246	1.00	11.06
ATOM	1946	CD1	LEU	246	22.614	2.285	35.841	1.00	10.74
ATOM	1947	CD2	LEU	246	20.108	2.158	35.515	1.00	11.92
ATOM	1948	C	LEU	246	19.442	3.277	39.711	1.00	13.39
ATOM	1949	O	LEU	246	20.212	2.652	40.468	1.00	14.42
ATOM	1950	N	VAL	247	18.321	3.862	40.110	1.00	12.95
ATOM	1951	CA	VAL	247	17.828	3.838	41.483	1.00	14.07
ATOM	1952	CB	VAL	247	17.234	5.200	41.833	1.00	14.69
ATOM	1953	CG1	VAL	247	16.472	5.110	43.156	1.00	16.48
ATOM	1954	CG2	VAL	247	18.363	6.239	41.922	1.00	16.18
ATOM	1955	C	VAL	247	16.780	2.749	41.538	1.00	14.37
ATOM	1956	O	VAL	247	15.835	2.753	40.747	1.00	13.95
ATOM	1957	N	GLU	248	16.937	1.810	42.468	1.00	15.26
ATOM	1958	CA	GLU	248	16.008	0.685	42.579	1.00	15.38
ATOM	1959	CB	GLU	248	16.439	-0.239	43.723	1.00	18.10
ATOM	1960	CG	GLU	248	15.585	-1.547	43.749	1.00	22.05
ATOM	1961	CD	GLU	248	16.403	-2.530	44.545	1.00	25.30
ATOM	1962	OE1	GLU	248	16.574	-2.268	45.755	1.00	27.75
ATOM	1963	OE2	GLU	248	16.872	-3.530	43.961	1.00	27.17
ATOM	1964	C	GLU	248	14.520	1.063	42.769	1.00	14.82
ATOM	1965	O	GLU	248	13.649	0.497	42.107	1.00	13.94
ATOM	1966	N	ASN	249	14.246	2.010	43.663	1.00	13.99
ATOM	1967	CA	ASN	249	12.878	2.435	43.925	1.00	14.73
ATOM	1968	CB	ASN	249	12.821	3.193	45.256	1.00	15.18
ATOM	1969	CG	ASN	249	11.435	3.822	45.519	1.00	16.41
ATOM	1970	OD1	ASN	249	10.499	3.664	44.728	1.00	16.50
ATOM	1971	ND2	ASN	249	11.312	4.528	46.643	1.00	16.98
ATOM	1972	C	ASN	249	12.447	3.336	42.759	1.00	13.11
ATOM	1973	O	ASN	249	12.961	4.438	42.611	1.00	14.63

FIG.11B-47

ATOM	1974	N	PRO	250	11.518	2.862	41.912	1.00	13.20
ATOM	1975	CD	PRO	250	10.763	1.599	42.012	1.00	12.72
ATOM	1976	CA	PRO	250	11.057	3.658	40.766	1.00	13.23
ATOM	1977	CB	PRO	250	10.079	2.706	40.055	1.00	13.24
ATOM	1978	CG	PRO	250	9.507	1.906	41.190	1.00	13.59
ATOM	1979	C	PRO	250	10.446	4.976	41.155	1.00	13.43
ATOM	1980	O	PRO	250	10.442	5.921	40.365	1.00	13.46
ATOM	1981	N	SER	251	9.904	5.050	42.368	1.00	14.06
ATOM	1982	CA	SER	251	9.303	6.302	42.803	1.00	15.63
ATOM	1983	CB	SER	251	8.386	6.059	44.002	1.00	15.27
ATOM	1984	OG	SER	251	7.238	5.337	43.589	1.00	15.42
ATOM	1985	C	SER	251	10.372	7.369	43.132	1.00	15.99
ATOM	1986	O	SER	251	10.099	8.558	43.044	1.00	19.15
ATOM	1987	N	ALA	252	11.577	6.933	43.480	1.00	16.36
ATOM	1988	CA	ALA	252	12.670	7.846	43.812	1.00	15.52
ATOM	1989	CB	ALA	252	13.504	7.261	44.950	1.00	15.97
ATOM	1990	C	ALA	252	13.568	8.099	42.602	1.00	14.86
ATOM	1991	O	ALA	252	14.398	9.002	42.603	1.00	16.55
ATOM	1992	N	ARG	253	13.407	7.279	41.577	1.00	14.26
ATOM	1993	CA	ARG	253	14.230	7.395	40.364	1.00	13.52
ATOM	1994	CB	ARG	253	13.892	6.245	39.416	1.00	13.08
ATOM	1995	CG	ARG	253	14.732	6.070	38.114	1.00	13.50
ATOM	1996	CD	ARG	253	14.277	4.765	37.436	1.00	12.90
ATOM	1997	NE	ARG	253	14.298	3.661	38.395	1.00	13.33
ATOM	1998	CZ	ARG	253	13.564	2.561	38.289	1.00	13.77
ATOM	1999	NH1	ARG	253	13.638	1.625	39.238	1.00	12.46
ATOM	2000	NH2	ARG	253	12.771	2.397	37.234	1.00	12.92
ATOM	2001	C	ARG	253	13.990	8.732	39.658	1.00	12.93
ATOM	2002	O	ARG	253	12.882	9.268	39.690	1.00	13.28
ATOM	2003	N	ILE	254	15.032	9.268	39.034	1.00	12.41
ATOM	2004	CA	ILE	254	14.927	10.544	38.329	1.00	12.24
ATOM	2005	CB	ILE	254	16.349	11.025	37.858	1.00	12.27
ATOM	2006	CG2	ILE	254	16.870	10.133	36.704	1.00	12.14
ATOM	2007	CG1	ILE	254	16.295	12.496	37.429	1.00	13.31
ATOM	2008	CD1	ILE	254	17.706	13.120	37.107	1.00	12.84
ATOM	2009	C	ILE	254	13.951	10.432	37.157	1.00	13.19
ATOM	2010	O	ILE	254	13.853	9.384	36.510	1.00	12.84
ATOM	2011	N	THR	255	13.209	11.510	36.909	1.00	12.98
ATOM	2012	CA	THR	255	12.264	11.570	35.804	1.00	14.49
ATOM	2013	CB	THR	255	11.020	12.385	36.186	1.00	15.98
ATOM	2014	OG1	THR	255	11.419	13.721	36.526	1.00	16.76
ATOM	2015	CG2	THR	255	10.342	11.754	37.390	1.00	16.72

FIG.11B-48

ATOM	2016	C	THR	255	12.962	12.266	34.662	1.00	14.89
ATOM	2017	O	THR	255	14.002	12.908	34.850	1.00	14.36
ATOM	2018	N	ILE	256	12.387	12.180	33.473	1.00	14.96
ATOM	2019	CA	ILE	256	13.022	12.822	32.338	1.00	15.85
ATOM	2020	CB	ILE	256	12.323	12.446	31.031	1.00	15.90
ATOM	2021	CG2	ILE	256	12.969	13.227	29.886	1.00	16.70
ATOM	2022	CG1	ILE	256	12.416	10.929	30.824	1.00	16.68
ATOM	2023	CD1	ILE	256	11.763	10.410	29.490	1.00	17.39
ATOM	2024	C	ILE	256	13.121	14.347	32.495	1.00	15.76
ATOM	2025	O	ILE	256	14.146	14.936	32.162	1.00	15.74
ATOM	2026	N	PRO	257	12.058	15.008	32.988	1.00	16.02
ATOM	2027	CD	PRO	257	10.663	14.579	33.216	1.00	16.52
ATOM	2028	CA	PRO	257	12.196	16.461	33.137	1.00	16.77
ATOM	2029	CB	PRO	257	10.845	16.869	33.730	1.00	16.80
ATOM	2030	CG	PRO	257	9.886	15.903	33.072	1.00	16.27
ATOM	2031	C	PRO	257	13.448	16.832	34.008	1.00	17.42
ATOM	2032	O	PRO	257	14.093	17.848	33.765	1.00	18.68
ATOM	2033	N	ASP	258	13.776	15.999	34.996	1.00	17.57
ATOM	2034	CA	ASP	258	14.934	16.252	35.857	1.00	17.40
ATOM	2035	CB	ASP	258	14.727	15.585	37.229	1.00	18.84
ATOM	2036	CG	ASP	258	13.770	16.499	38.040	1.00	20.18
ATOM	2037	OD1	ASP	258	13.098	16.010	38.969	1.00	19.96
ATOM	2038	OD2	ASP	258	13.710	17.711	37.743	1.00	22.03
ATOM	2039	C	ASP	258	16.254	15.810	35.165	1.00	16.71
ATOM	2040	O	ASP	258	17.313	16.400	35.402	1.00	17.53
ATOM	2041	N	ILE	259	16.180	14.792	34.312	1.00	16.00
ATOM	2042	CA	ILE	259	17.361	14.357	33.567	1.00	14.73
ATOM	2043	CB	ILE	259	17.061	13.134	32.658	1.00	13.25
ATOM	2044	CG2	ILE	259	18.186	12.932	31.636	1.00	11.56
ATOM	2045	CG1	ILE	259	16.926	11.870	33.512	1.00	13.50
ATOM	2046	CD1	ILE	259	16.359	10.635	32.718	1.00	14.05
ATOM	2047	C	ILE	259	17.777	15.511	32.650	1.00	15.65
ATOM	2048	O	ILE	259	18.956	15.768	32.455	1.00	15.76
ATOM	2049	N	LYS	260	16.801	16.225	32.097	1.00	17.80
ATOM	2050	CA	LYS	260	17.134	17.318	31.195	1.00	19.60
ATOM	2051	CB	LYS	260	15.882	17.772	30.437	1.00	21.62
ATOM	2052	CG	LYS	260	14.787	18.292	31.278	1.00	25.24
ATOM	2053	CD	LYS	260	13.557	18.718	30.460	1.00	27.14
ATOM	2054	CE	LYS	260	12.448	19.266	31.394	1.00	28.28
ATOM	2055	NZ	LYS	260	13.018	20.136	32.457	1.00	28.09
ATOM	2056	C	LYS	260	17.787	18.495	31.910	1.00	19.77
ATOM	2057	O	LYS	260	18.302	19.412	31.258	1.00	19.52

FIG.11B-49

ATOM	2058	N	LYS	261	17.769	18.465	33.244	1.00	19.58
ATOM	2059	CA	LYS	261	18.377	19.513	34.063	1.00	20.76
ATOM	2060	CB	LYS	261	17.441	19.911	35.207	1.00	22.07
ATOM	2061	CG	LYS	261	16.225	20.617	34.640	1.00	24.13
ATOM	2062	CD	LYS	261	15.304	20.904	35.853	1.00	25.66
ATOM	2063	CE	LYS	261	13.996	21.718	35.627	1.00	27.76
ATOM	2064	NZ	LYS	261	14.253	23.180	35.441	1.00	29.98
ATOM	2065	C	LYS	261	19.708	19.078	34.677	1.00	19.39
ATOM	2066	O	LYS	261	20.398	19.877	35.320	1.00	20.44
ATOM	2067	N	ASP	262	20.075	17.817	34.461	1.00	17.11
ATOM	2068	CA	ASP	262	21.307	17.258	35.002	1.00	16.68
ATOM	2069	CB	ASP	262	21.348	15.747	34.725	1.00	15.81
ATOM	2070	CG	ASP	262	22.727	15.133	34.962	1.00	15.09
ATOM	2071	OD1	ASP	262	23.534	15.000	34.021	1.00	15.37
ATOM	2072	OD2	ASP	262	23.049	14.765	36.105	1.00	15.37
ATOM	2073	C	ASP	262	22.539	17.953	34.484	1.00	16.67
ATOM	2074	O	ASP	262	22.595	18.357	33.322	1.00	15.94
ATOM	2075	N	ARG	263	23.535	18.094	35.353	1.00	16.49
ATOM	2076	CA	ARG	263	24.781	18.773	34.997	1.00	17.66
ATOM	2077	CB	ARG	263	25.751	18.741	36.179	1.00	19.91
ATOM	2078	CG	ARG	263	27.046	19.552	35.881	1.00	23.77
ATOM	2079	CD	ARG	263	27.952	19.734	37.161	1.00	26.98
ATOM	2080	NE	ARG	263	28.878	18.625	37.404	1.00	30.04
ATOM	2081	CZ	ARG	263	28.535	17.410	37.833	1.00	31.76
ATOM	2082	NH1	ARG	263	27.264	17.108	38.076	1.00	32.73
ATOM	2083	NH2	ARG	263	29.476	16.495	38.044	1.00	32.79
ATOM	2084	C	ARG	263	25.481	18.182	33.763	1.00	16.93
ATOM	2085	O	ARG	263	25.873	18.915	32.858	1.00	17.03
ATOM	2086	N	TRP	264	25.643	16.864	33.725	1.00	15.70
ATOM	2087	CA	TRP	264	26.297	16.256	32.577	1.00	14.73
ATOM	2088	CB	TRP	264	26.576	14.770	32.818	1.00	14.69
ATOM	2089	CG	TRP	264	27.266	14.159	31.637	1.00	13.54
ATOM	2090	CD2	TRP	264	26.677	13.327	30.637	1.00	13.29
ATOM	2091	CE2	TRP	264	27.683	13.043	29.683	1.00	13.31
ATOM	2092	CE3	TRP	264	25.390	12.789	30.448	1.00	13.02
ATOM	2093	CD1	TRP	264	28.568	14.345	31.264	1.00	13.98
ATOM	2094	NE1	TRP	264	28.823	13.679	30.092	1.00	12.82
ATOM	2095	CZ2	TRP	264	27.448	12.244	28.556	1.00	13.12
ATOM	2096	CZ3	TRP	264	25.157	11.997	29.329	1.00	11.93
ATOM	2097	CH2	TRP	264	26.178	11.731	28.397	1.00	11.95
ATOM	2098	C	TRP	264	25.437	16.398	31.287	1.00	14.29
ATOM	2099	O	TRP	264	25.954	16.683	30.199	1.00	13.06

FIG.11B-50

ATOM	2100	N	TYR	265	24.132	16.217	31.427	1.00	14.18
ATOM	2101	CA	TYR	265	23.228	16.327	30.287	1.00	14.24
ATOM	2102	CB	TYR	265	21.779	16.158	30.753	1.00	14.67
ATOM	2103	CG	TYR	265	20.786	16.027	29.623	1.00	14.92
ATOM	2104	CD1	TYR	265	20.225	17.150	29.014	1.00	15.83
ATOM	2105	CE1	TYR	265	19.303	17.016	27.971	1.00	16.00
ATOM	2106	CD2	TYR	265	20.404	14.768	29.161	1.00	15.34
ATOM	2107	CE2	TYR	265	19.492	14.627	28.124	1.00	15.43
ATOM	2108	CZ	TYR	265	18.948	15.747	27.540	1.00	16.30
ATOM	2109	OH	TYR	265	18.056	15.596	26.517	1.00	17.21
ATOM	2110	C	TYR	265	23.420	17.698	29.574	1.00	14.08
ATOM	2111	O	TYR	265	23.402	17.782	28.340	1.00	13.66
ATOM	2112	N	ASN	266	23.638	18.743	30.367	1.00	14.50
ATOM	2113	CA	ASN	266	23.816	20.093	29.832	1.00	15.04
ATOM	2114	CB	ASN	266	23.127	21.112	30.744	1.00	16.27
ATOM	2115	CG	ASN	266	21.623	20.873	30.628	1.00	17.50
ATOM	2116	OD1	ASN	266	21.019	21.164	29.595	1.00	18.67
ATOM	2117	ND2	ASN	266	21.017	20.324	31.689	1.00	17.20
ATOM	2118	C	ASN	266	25.283	20.545	29.665	1.00	15.81
ATOM	2119	O	ASN	266	25.551	21.696	29.333	1.00	15.28
ATOM	2120	N	LYS	267	26.229	19.639	29.867	1.00	15.30
ATOM	2121	CA	LYS	267	27.626	20.022	29.739	1.00	16.63
ATOM	2122	CB	LYS	267	28.510	19.009	30.468	1.00	18.26
ATOM	2123	CG	LYS	267	29.969	19.316	30.381	1.00	18.95
ATOM	2124	CD	LYS	267	30.607	18.191	31.212	1.00	20.54
ATOM	2125	CE	LYS	267	32.097	18.519	31.285	1.00	21.22
ATOM	2126	NZ	LYS	267	32.271	19.896	31.837	1.00	25.63
ATOM	2127	C	LYS	267	28.096	20.128	28.280	1.00	17.13
ATOM	2128	O	LYS	267	27.925	19.200	27.491	1.00	17.02
ATOM	2129	N	PRO	268	28.668	21.285	27.899	1.00	17.19
ATOM	2130	CD	PRO	268	28.680	22.567	28.624	1.00	18.04
ATOM	2131	CA	PRO	268	29.151	21.449	26.525	1.00	18.03
ATOM	2132	CB	PRO	268	29.594	22.914	26.489	1.00	18.73
ATOM	2133	CG	PRO	268	28.717	23.576	27.485	1.00	18.08
ATOM	2134	C	PRO	268	30.291	20.455	26.275	1.00	19.66
ATOM	2135	O	PRO	268	31.263	20.407	27.041	1.00	18.33
ATOM	2136	N	LEU	269	30.183	19.688	25.196	1.00	20.60
ATOM	2137	CA	LEU	269	31.191	18.680	24.884	1.00	23.11
ATOM	2138	CB	LEU	269	30.735	17.287	25.326	1.00	21.93
ATOM	2139	CG	LEU	269	30.429	16.951	26.782	1.00	21.11
ATOM	2140	CD1	LEU	269	29.824	15.559	26.864	1.00	20.44
ATOM	2141	CD2	LEU	269	31.709	17.029	27.611	1.00	21.85

FIG.11B-51

ATOM	2142	C	LEU	269	31.519	18.481	23.398	1.00	25.42
ATOM	2143	O	LEU	269	32.694	18.357	23.024	1.00	25.84
ATOM	2144	N	LYS	270	30.478	18.456	22.572	1.00	28.13
ATOM	2145	CA	LYS	270	30.638	18.172	21.148	1.00	31.59
ATOM	2146	CB	LYS	270	29.792	16.951	20.777	1.00	32.48
ATOM	2147	CG	LYS	270	29.974	16.336	19.385	1.00	34.36
ATOM	2148	CD	LYS	270	29.245	14.976	19.311	1.00	34.97
ATOM	2149	CE	LYS	270	29.342	14.378	17.904	1.00	36.24
ATOM	2150	NZ	LYS	270	28.578	13.107	17.794	1.00	37.61
ATOM	2151	C	LYS	270	30.326	19.247	20.152	1.00	32.71
ATOM	2152	O	LYS	270	29.331	19.965	20.267	1.00	33.61
ATOM	2153	N	LYS	271	31.182	19.353	19.143	1.00	34.01
ATOM	2154	CA	LYS	271	30.984	20.338	18.093	1.00	34.65
ATOM	2155	CB	LYS	271	32.296	20.639	17.364	1.00	34.43
ATOM	2156	CG	LYS	271	33.612	21.016	18.114	1.00	34.00
ATOM	2157	CD	LYS	271	33.425	21.680	19.493	1.00	32.78
ATOM	2158	CE	LYS	271	34.683	22.342	20.087	1.00	32.43
ATOM	2159	NZ	LYS	271	34.911	23.689	19.493	1.00	29.16
ATOM	2160	C	LYS	271	30.002	19.770	17.100	1.00	35.51
ATOM	2161	O	LYS	271	29.873	18.545	16.970	1.00	35.67
ATOM	2162	N	GLY	272	29.304	20.653	16.392	1.00	36.22
ATOM	2163	CA	GLY	272	28.334	20.207	15.412	1.00	37.58
ATOM	2164	C	GLY	272	28.974	19.331	14.357	1.00	38.77
ATOM	2165	O	GLY	272	30.181	19.085	14.392	1.00	39.05
ATOM	2166	N	ALA	273	28.165	18.859	13.415	1.00	39.07
ATOM	2167	CA	ALA	273	28.663	18.004	12.347	1.00	39.69
ATOM	2168	CB	ALA	273	27.559	17.736	11.334	1.00	39.13
ATOM	2169	C	ALA	273	29.834	18.652	11.667	1.00	40.12
ATOM	2170	O	ALA	273	30.138	19.821	11.907	1.00	40.27
ATOM	2171	N	ALA	274	30.506	17.889	10.811	1.00	40.80
ATOM	2172	CA	ALA	274	31.650	18.406	10.075	1.00	41.43
ATOM	2173	CB	ALA	274	32.667	17.297	9.834	1.00	41.17
ATOM	2174	C	ALA	274	31.149	18.955	8.761	1.00	41.68
ATOM	2175	O	ALA	274	30.049	18.613	8.317	1.00	42.49
ATOM	2176	N	ALA	275	31.947	19.820	8.143	1.00	41.82
ATOM	2177	CA	ALA	275	31.600	20.428	6.860	1.00	41.71
ATOM	2178	CB	ALA	275	31.811	19.414	5.741	1.00	41.41
ATOM	2179	C	ALA	275	30.158	20.973	6.807	1.00	41.89
ATOM	2180	O	ALA	275	29.423	20.708	5.850	1.00	42.04
ATOM	2181	N	ALA	276	29.767	21.733	7.829	1.00	41.67
ATOM	2182	CA	ALA	276	28.425	22.310	7.881	1.00	41.71
ATOM	2183	CB	ALA	276	27.377	21.201	7.836	1.00	40.99

FIG.11B-52

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ATOM   2184  C    ALA   276      28.226  23.157   9.127  1.00 41.84
ATOM   2185  O    ALA   276      28.106  24.394   9.001  1.00 42.24
ATOM   2186  OT   ALA   276      28.190  22.590  10.239  1.00 42.70
ATOM   2187  OH2 WAT   500       7.427  -2.493  31.016  1.00 12.44
ATOM   2188  OH2 WAT   501       7.228   0.472  30.486  1.00 11.40
ATOM   2189  OH2 WAT   502       8.194   1.752  37.455  1.00 11.41
ATOM   2190  OH2 WAT   503      12.286  -2.112  29.696  1.00 12.42
ATOM   2191  OH2 WAT   504      12.428  -0.037  27.883  1.00 11.16
ATOM   2192  OH2 WAT   505       8.356  10.402  31.031  1.00 13.84
ATOM   2193  OH2 WAT   507      15.558  -3.663  26.632  1.00 12.28
ATOM   2194  OH2 WAT   508       6.988   4.420  40.772  1.00 14.28
ATOM   2195  OH2 WAT   509      11.678   7.753  36.355  1.00 15.05
ATOM   2196  OH2 WAT   510       9.743  10.806  33.175  1.00 13.52
ATOM   2197  OH2 WAT   511      14.137  -4.264  28.939  1.00 11.96
ATOM   2198  OH2 WAT   512      12.161  -1.918  42.464  1.00 17.92
ATOM   2199  OH2 WAT   513      23.034  -4.599  32.333  1.00 14.48
ATOM   2200  OH2 WAT   514      13.701  -1.328  31.829  1.00 13.65
ATOM   2201  OH2 WAT   515       7.725   2.793  44.539  1.00 13.92
ATOM   2202  OH2 WAT   516      10.498   8.123  38.870  1.00 18.75
ATOM   2203  OH2 WAT   517       8.458  -2.193  21.559  1.00 15.87
ATOM   2204  OH2 WAT   518       3.854  -8.500  37.109  1.00 21.28
ATOM   2205  OH2 WAT   519       6.585  13.179  28.016  1.00 15.92
ATOM   2206  OH2 WAT   520       4.308   6.179  34.254  1.00 14.46
ATOM   2207  OH2 WAT   521      -2.497   7.216  24.331  1.00 20.93
ATOM   2208  OH2 WAT   522      25.696  14.974  36.359  1.00 15.50
ATOM   2209  OH2 WAT   523      10.006  -1.183  44.079  1.00 17.12
ATOM   2210  OH2 WAT   524      18.801  -3.771  34.262  1.00 12.85
ATOM   2211  OH2 WAT   525       9.859  -3.573  29.813  1.00 12.22
ATOM   2212  OH2 WAT   526      23.813  -2.488  12.469  1.00 24.20
ATOM   2213  OH2 WAT   527      33.619   6.620  29.594  1.00 13.33
ATOM   2214  OH2 WAT   528      12.025  -0.860  12.686  1.00 16.92
ATOM   2215  OH2 WAT   529       5.067  -3.939  31.031  1.00 15.55
ATOM   2216  OH2 WAT   530      16.206   2.905  45.578  1.00 21.26
ATOM   2217  OH2 WAT   531       6.508   1.842  39.468  1.00 13.83
ATOM   2218  OH2 WAT   532       9.848  -0.013  13.922  1.00 16.77
ATOM   2219  OH2 WAT   533       8.482  13.036  29.893  1.00 21.35
ATOM   2220  OH2 WAT   534       1.955   3.242  33.881  1.00 14.23
ATOM   2221  OH2 WAT   535       8.004   9.104  38.937  1.00 20.33
ATOM   2222  OH2 WAT   536       9.589   8.422  34.802  1.00 13.64
ATOM   2223  OH2 WAT   538      13.208  13.372  39.318  1.00 17.18
ATOM   2224  OH2 WAT   539      12.245  -5.696  20.845  1.00 19.96
ATOM   2225  OH2 WAT   540      11.065  -3.376  13.747  1.00 23.19
```

FIG.11B-53

ATOM	2226	OH2	WAT	542	10.329	-0.437	-17.113	1.00 15.49
ATOM	2227	OH2	WAT	543	34.999	12.972	30.493	1.00 20.46
ATOM	2228	OH2	WAT	544	6.038	-4.021	-15.260	1.00 18.16
ATOM	2229	OH2	WAT	545	2.722	-3.465	20.201	1.00 22.45
ATOM	2230	OH2	WAT	546	23.120	17.680	38.118	1.00 21.95
ATOM	2231	OH2	WAT	547	4.224	12.544	29.399	1.00 22.88
ATOM	2232	OH2	WAT	548	27.520	19.070	23.817	1.00 18.56
ATOM	2233	OH2	WAT	549	11.453	0.217	-14.778	1.00 18.21
ATOM	2234	OH2	WAT	550	8.159	8.888	13.504	1.00 22.71
ATOM	2235	OH2	WAT	551	7.518	-1.202	14.804	1.00 19.40
ATOM	2236	OH2	WAT	552	25.729	0.976	13.336	1.00 25.24
ATOM	2237	OH2	WAT	553	8.421	2.347	13.686	1.00 18.49
ATOM	2238	OH2	WAT	554	32.146	14.746	31.790	1.00 16.58
ATOM	2239	OH2	WAT	555	10.588	15.422	22.583	1.00 20.42
ATOM	2240	OH2	WAT	556	-7.789	5.192	30.091	1.00 21.72
ATOM	2241	OH2	WAT	557	24.235	11.751	41.632	1.00 23.21
ATOM	2242	OH2	WAT	558	13.097	5.532	4.167	1.00 22.65
ATOM	2243	OH2	WAT	561	7.327	8.904	36.362	1.00 19.07
ATOM	2244	OH2	WAT	562	5.298	7.204	36.854	1.00 19.10
ATOM	2245	OH2	WAT	563	17.888	14.061	15.698	1.00 28.05
ATOM	2246	OH2	WAT	564	5.803	10.952	34.891	1.00 25.56
ATOM	2247	OH2	WAT	565	19.385	-8.096	22.747	1.00 27.33
ATOM	2248	OH2	WAT	567	-5.961	9.687	24.986	1.00 28.68
ATOM	2249	OH2	WAT	568	12.502	16.572	24.587	1.00 24.90
ATOM	2250	OH2	WAT	569	4.420	13.953	22.823	1.00 19.89
ATOM	2251	OH2	WAT	570	6.037	16.089	27.263	1.00 27.33
ATOM	2252	OH2	WAT	571	0.295	-4.830	31.670	1.00 22.95
ATOM	2253	OH2	WAT	572	5.126	7.073	43.112	1.00 26.68
ATOM	2254	OH2	WAT	573	7.925	12.617	34.293	1.00 19.25
ATOM	2255	OH2	WAT	574	2.838	8.548	37.282	1.00 22.58
ATOM	2256	OH2	WAT	575	6.541	6.869	39.585	1.00 20.25
ATOM	2257	OH2	WAT	577	16.348	13.014	13.638	1.00 21.44
ATOM	2258	OH2	WAT	578	20.689	-11.863	31.456	1.00 22.24
ATOM	2259	OH2	WAT	579	28.216	-3.073	39.433	1.00 23.94
ATOM	2260	OH2	WAT	580	4.817	12.316	31.998	1.00 24.78
ATOM	2261	OH2	WAT	582	2.495	10.173	33.047	1.00 25.54
ATOM	2262	OH2	WAT	584	9.873	-9.843	26.499	1.00 22.35
ATOM	2263	OH2	WAT	585	18.849	6.343	6.565	1.00 23.80
ATOM	2264	OH2	WAT	586	5.936	15.554	24.398	1.00 32.00
ATOM	2265	OH2	WAT	587	7.942	15.782	22.364	1.00 28.34
ATOM	2266	OH2	WAT	588	6.895	14.265	32.126	1.00 25.39
ATOM	2267	OH2	WAT	589	-0.295	-3.712	42.925	1.00 25.73

FIG.11B-54

ATOM	2268	OH2	WAT	590	-3.936	9.005	35.847	1.00 24.10
ATOM	2269	OH2	WAT	591	18.913	2.038	44.494	1.00 26.21
ATOM	2270	OH2	WAT	592	28.625	-6.540	28.424	1.00 26.01
ATOM	2271	OH2	WAT	593	26.141	-9.992	35.885	1.00 25.72
ATOM	2272	OH2	WAT	594	-4.117	0.747	36.348	1.00 21.02
ATOM	2273	OH2	WAT	595	4.898	-5.492	46.334	1.00 25.89
ATOM	2274	OH2	WAT	596	-1.825	-3.880	35.982	1.00 26.80
ATOM	2275	OH2	WAT	597	17.281	-10.153	23.419	1.00 29.07
ATOM	2276	OH2	WAT	598	6.074	7.250	12.492	1.00 26.52
ATOM	2277	OH2	WAT	599	14.343	0.413	-12.155	1.00 26.20
ATOM	2278	OH2	WAT	600	5.724	-15.362	35.592	1.00 31.55
ATOM	2279	OH2	WAT	601	31.405	-5.699	25.906	1.00 31.89
ATOM	2280	OH2	WAT	602	19.144	16.433	37.632	1.00 27.84
ATOM	2281	OH2	WAT	604	-1.682	10.834	26.579	1.00 25.33
ATOM	2282	OH2	WAT	605	7.446	14.038	36.610	1.00 31.51
ATOM	2283	OH2	WAT	606	8.931	-11.385	28.785	1.00 31.07
ATOM	2284	OH2	WAT	607	2.276	13.259	17.394	1.00 29.99
ATOM	2285	OH2	WAT	608	10.037	-6.636	-8.218	1.00 29.41
ATOM	2286	OH2	WAT	609	25.470	-3.163	24.453	1.00 36.33
ATOM	2287	OH2	WAT	610	5.918	-3.633	-5.105	1.00 29.98
ATOM	2288	OH2	WAT	611	22.980	-14.777	33.710	1.00 37.86
ATOM	2289	OH2	WAT	612	29.084	-4.501	37.176	1.00 26.11
ATOM	2290	OH2	WAT	613	34.969	-5.345	38.036	1.00 36.77
ATOM	2291	OH2	WAT	614	22.538	-5.866	24.355	1.00 25.61
ATOM	2292	OH2	WAT	615	2.677	5.500	42.779	1.00 22.04
ATOM	2293	OH2	WAT	616	-1.262	-0.266	1.007	1.00 41.96
ATOM	2294	OH2	WAT	617	14.838	-2.729	15.686	1.00 26.97
ATOM	2295	OH2	WAT	618	7.254	-5.958	-4.621	1.00 32.47
ATOM	2296	OH2	WAT	619	14.437	-0.485	-7.588	1.00 24.67
ATOM	2297	OH2	WAT	620	13.993	16.537	27.899	1.00 37.44
ATOM	2298	OH2	WAT	621	35.859	6.788	17.703	1.00 36.41
ATOM	2299	OH2	WAT	622	1.225	3.363	-11.071	1.00 34.68
ATOM	2300	OH2	WAT	623	17.438	12.289	41.236	1.00 24.21
ATOM	2301	OH2	WAT	624	21.271	-0.227	7.878	1.00 33.25
ATOM	2302	OH2	WAT	625	6.639	15.315	16.521	1.00 33.67
ATOM	2303	OH2	WAT	626	6.373	4.916	13.973	1.00 25.91
ATOM	2304	OH2	WAT	627	3.444	-2.333	-2.127	1.00 34.16
ATOM	2305	OH2	WAT	628	8.270	-6.751	16.481	1.00 27.56
ATOM	2306	OH2	WAT	629	15.541	13.948	41.048	1.00 29.49
ATOM	2307	OH2	WAT	630	23.084	16.734	21.168	1.00 26.00
ATOM	2308	OH2	WAT	631	19.690	5.426	-11.485	1.00 25.65
ATOM	2309	OH2	WAT	632	2.999	1.453	-10.337	1.00 32.88

FIG.11B-55

ATOM	2310	OH2	WAT	633	-10.039	6.144	37.785	1.00	32.06
ATOM	2311	OH2	WAT	634	25.680	21.534	32.761	1.00	30.38
ATOM	2312	OH2	WAT	636	1.101	14.667	27.285	1.00	33.90
ATOM	2313	OH2	WAT	637	4.677	-7.995	15.521	1.00	39.69
ATOM	2314	OH2	WAT	638	-4.199	10.629	27.487	1.00	25.74
ATOM	2315	OH2	WAT	639	16.727	16.185	23.380	1.00	24.68
ATOM	2316	OH2	WAT	641	4.762	8.324	41.074	1.00	32.42
ATOM	2317	OH2	WAT	642	1.346	-0.850	-3.508	1.00	37.14
ATOM	2318	OH2	WAT	643	6.494	-5.448	-2.382	1.00	29.92
ATOM	2319	OH2	WAT	644	-0.637	10.395	17.913	1.00	32.31
ATOM	2320	OH2	WAT	645	28.896	-3.506	20.216	1.00	28.05
ATOM	2321	OH2	WAT	646	13.649	-8.354	22.832	1.00	36.52
ATOM	2322	OH2	WAT	647	-4.016	-2.000	41.527	1.00	41.51
ATOM	2323	OH2	WAT	648	-3.699	4.194	15.863	1.00	34.38
ATOM	2324	OH2	WAT	649	18.236	9.536	44.036	1.00	40.10
ATOM	2325	OH2	WAT	650	-2.251	-2.420	29.819	1.00	37.50
ATOM	2326	OH2	WAT	651	28.245	9.734	16.414	1.00	31.59
ATOM	2327	OH2	WAT	652	25.887	14.410	11.861	1.00	39.37
ATOM	2328	OH2	WAT	653	-4.668	-3.492	21.738	1.00	38.13
ATOM	2329	OH2	WAT	654	15.932	8.831	-4.665	1.00	42.38
ATOM	2330	OH2	WAT	655	39.349	-0.041	40.457	1.00	36.11
ATOM	2331	OH2	WAT	656	16.291	15.362	18.684	1.00	28.74
ATOM	2332	OH2	WAT	657	20.650	8.704	43.546	1.00	26.18
ATOM	2333	OH2	WAT	658	21.731	4.870	-9.446	1.00	41.19
ATOM	2334	OH2	WAT	659	27.579	-8.698	29.528	1.00	36.99
ATOM	2335	OH2	WAT	660	15.065	1.058	-9.945	1.00	34.45
ATOM	2336	C1	ADPN	800	15.589	-7.036	12.366	1.00	29.43
ATOM	2337	C2	ADPN	800	16.795	-6.562	11.567	1.00	27.99
ATOM	2338	O1	ADPN	800	16.276	-5.540	10.684	1.00	26.79
ATOM	2339	C3	ADPN	800	17.832	-5.869	12.464	1.00	28.23
ATOM	2340	O2	ADPN	800	19.138	-6.070	11.920	1.00	29.48
ATOM	2341	C4	ADPN	800	17.379	-4.406	12.439	1.00	27.06
ATOM	2342	O3	ADPN	800	18.452	-3.550	12.841	1.00	29.12
ATOM	2343	C5	ADPN	800	16.915	-4.275	10.979	1.00	25.84
ATOM	2344	N1	ADPN	800	15.939	-3.162	10.843	1.00	23.38
ATOM	2345	C6	ADPN	800	14.655	-3.121	11.351	1.00	23.14
ATOM	2346	N2	ADPN	800	14.038	-1.962	10.976	1.00	22.86
ATOM	2347	C7	ADPN	800	14.938	-1.266	10.236	1.00	22.16
ATOM	2348	C8	ADPN	800	14.895	-0.025	9.594	1.00	22.13
ATOM	2349	N3	ADPN	800	13.812	0.764	9.707	1.00	21.32
ATOM	2350	N4	ADPN	800	16.025	0.390	8.889	1.00	21.64
ATOM	2351	C9	ADPN	800	17.152	-0.341	8.819	1.00	21.90

FIG.11B-56

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ATOM   2352  N5  ADPN  800      17.271  -1.548   9.430  1.00 21.98
ATOM   2353  C10 ADPN  800      16.144  -2.011  10.140  1.00 22.86
ATOM   2354  S   S04   901      -0.220  -4.850  27.961  1.00 26.12
ATOM   2355  01  S04   901       0.507  -5.374  26.794  1.00 26.13
ATOM   2356  02  S04   901       0.700  -4.720  29.109  1.00 28.87
ATOM   2357  03  S04   901      -1.308  -5.781  28.341  1.00 24.66
ATOM   2358  04  S04   901      -0.818  -3.538  27.657  1.00 29.71
END
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FIG.11B-57

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(54) Catalytic domain of the human effector cell cycle checkpoint protein kinase, Chk1, materials and methods for identification of inhibitors thereof

(57) The present invention relates to the identification, isolation and purification of the catalytic domain of the human effector checkpoint protein kinase (hChk1). A 1.7Ô crystal structure of the hChk1 kinase domain in the active conformation is reported herein. The kinase domain of hChk1 and its associated crystal structure is described for use in the discovery, identification and characterization of inhibitors of hChk1. This structure provides a three-dimensional description of the binding site of the hChk1 for structure-based design of small molecule inhibitors thereof as therapeutic agents. Inhibitors of hChk1 find utility in the treatment of hyperproliferative disorders such as HIV and cancer.

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European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 00 12 3738

DOCUMENTS CONSIDERED TO BE RELEVANT

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X Y	WO 99 11795 A (CARR ANTONY MICHAEL ;ICOS CORP (US)) 11 March 1999 (1999-03-11) * the whole document * Seq. Id. Nos. 1 and 2 show 100% and 99% identity to Seq. d. Nos. 1 and 2, respectively * claims 1-29; examples 1,6 *	1,2, 14-40 3-13,41	C12N15/54 C12N9/12 C12Q1/34
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TECHNICAL FIELDS SEARCHED (Int.Cl.7)
C12N
C12Q

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
MUNICH	25 July 2002	Petri, B

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
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A : technological background
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& : member of the same patent family, corresponding document

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EUROPEAN SEARCH REPORT

Application Number
EP 00 12 3738

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Place of search	Date of completion of the search	Examiner
MUNICH	25 July 2002	Petri, B

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
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